UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

MEMORANDUM
Date: August 5, 2014

SUBJECT: Pirimiphos-methyl: Benchmark Dose Analysis of Acute and Subchronic Studies to Support Derivation of Points of Departure.

PC Code: 108102
Decision No.: 477390
Petition No.: NA
Risk Assessment Type: NA
TXR No.: 0057027
MRID No.: NA

DP Barcode: D420651
Registration No.: NA
Regulatory Action: Registration Review
Case No.: 2535
CAS No.: 29232-93-7
40 CFR: 180.409

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I. CONCLUSIONS

HED performed benchmark dose (BMD) analyses of several acute and subchronic studies for pirimiphos-methyl in order to support derivation of points of departure (POD) for pirimiphos-methyl as part of the single-chemical registration review risk assessment.

This memo summarizes the approach and presents the results of BMD analyses.

II. BACKGROUND

BMD analyses were performed with EPA's Benchmark Dose Software (Version 2.2) using an exponential model for continuous data. The data selected for evaluation consisted of decreased brain and red blood cell (RBC) cholinesterase (ChE) activities. For the acute studies, the analyses focused on adult data from an acute neurotoxicity study and both pup and adult data from the comparative cholinesterase (CCA) studies that entailed single dose exposures. Data from the 11-day repeated dosing and gestational dosing in the CCA study were also evaluated. In addition, OPP evaluated data from subchronic (oral and dermal), chronic, and developmental studies which included brain and/or RBC acetylcholinesterase (AChE) data in adult animals. AChE data from OP exposures ranging from approximately 21 days of dosing and longer are considered to be at steady state.

OPP has used the exponential model for modeling AChE activity for the OP and *N*-methyl carbamate cumulative risk assessments along with multiple single chemical risk assessments of ChE-inhibiting pesticides. Model runs for ChE activity were conducted with an appropriate benchmark response level (10%). As such the BMD_{10} (estimated dose to result in 10% change from background levels) and $BMDL_{10}$ (the lower 95% confidence level on the BMD_{10}) are provided in the output. Statistical (e.g., goodness of fit values) and graphical results were used in model evaluation.

III. RESULTS

The results of the single dose and repeated oral dosing BMD analyses are summarized below in Tables 1 and 2 respectively. Details are included in the appendix. Good model fit ($p>0.1$) was obtained for the majority of the analyses, with any exceptions being noted in these summary tables.

TABLE 1: Results of BMD Exponential Modeling for Brain and RBC ChE Data on Pirimiphos-methyl, Single Dose Studies

MRID/Study Title	Sex/Age	Compartment	BMD Results	
			BMD10 (mg/kg)	BMDL10 (mg/kg)
MRID 49037404 Acute CCA Study – Single Dose	Male Adult	RBC	38.35	30.76
MRID 49037404 Acute CCA Study – Single Dose	Female Adult	RBC	33.20	22.59
MRID 49037404 Acute CCA Study – Single Dose	Male Adult	Brain	185.19	121.52
MRID 49037404 Acute CCA Study – Single Dose	Female Adult	Brain	143.59	108.86
MRID 49037404 Acute CCA Study – Single Dose	Male Pup PND12	RBC	7.06	6.07
MRID 49037404 Acute CCA Study – Single Dose	Female Pup PND12	RBC	7.78	7.07
MRID 49037404 Acute CCA Study – Single Dose	Male Pup PND12	Brain	10.35	8.77
MRID 49037404 Acute CCA Study – Single Dose	Female Pup PND12	Brain	14.50	12.84
MRID 43594101 Acute Neurotoxicity – Single Dose	Male Adult Day 1	RBC	No adequate fit	No adequate fit
MRID 43594101	Female Adult Day 1	RBC	66.25	45.25

MRID/Study Title	Sex/Age	Compartment	BMD Results	
			BMD10 (mg/kg)	BMDL10 (mg/kg)
Acute Neurotoxicity – Single Dose				
MRID 43594101 Acute Neurotoxicity – Single Dose	Male Adult Day 15	RBC	98.84	15.22
MRID 43594101 Acute Neurotoxicity – Single Dose	Male Adult Day 1	Midbrain	No adequate fit	No adequate fit
MRID 43594101 Acute Neurotoxicity – Single Dose	Female Adult Day 1	Midbrain	82.89	63.52
MRID 43594101 Acute Neurotoxicity – Single Dose	Male Adult Day 1	Brainstem	81.41	57.97
MRID 43594101 Acute Neurotoxicity – Single Dose	Female Adult Day 1	Brainstem	88.11	63.58
MRID 43594101 Acute Neurotoxicity – Single Dose	Male Adult Day 1	Cerebellum	44.60	36.35
MRID 43594101 Acute Neurotoxicity – Single Dose	Female Adult Day 1	Cerebellum	44.43	37.32

TABLE 2: Results of BMD Exponential Modeling for Brain and RBC ChE Data on Pirimiphos-methyl, Repeated Oral Dosing Studies Ranging in Duration from 11 to 90 days.

MRID/Study Title	Sex/Age	Compartment	BMD Results	
			BMD10 (mg/kg)	BMDL10 (mg/kg)
MRID 49037406 Repeat CCA Study – 11 Days	Male Adult	RBC	2.63	2.03
MRID 49037406 Repeat CCA Study – 11 Days	Female Adult	RBC	1.64	1.28
MRID 49037406 Repeat CCA Study – 11 Days	Male Adult	Brain	15.98	12.66
MRID 49037406 Repeat CCA Study – 11 Days	Female Adult	Brain	5.51	3.92
MRID 49037406 Repeat CCA Study – 11 Days	Male Pup PND21	RBC	2.33[a]	0.98[a]
MRID 49037406 Repeat CCA Study – 11 Days	Female Pup PND21	RBC	1.01	0.73
MRID 49037406 Repeat CCA Study – 11 Days	Male Pup PND21	Brain	4.80[a]	3.93[a]
MRID 49037406 Repeat CCA Study – 11 Days	Female Pup PND21	Brain	3.69	2.92
MRID 43608201 Subchronic Neurotoxicity (90 days)	Male Adult Week 3	RBC	1.20	0.68

MRID/Study Title	Sex/Age	Compartment	BMD Results	
			BMD10 (mg/kg)	BMDL10 (mg/kg)
MRID 43608201 Subchronic Neurotoxicity in Rats (90 days)	Female Adult Week 7	RBC	4.33	3.41
MRID 43608201 Subchronic Neurotoxicity in Rats (90 days)	Male Adult Week 13	RBC	4.66	3.60
MRID 43608201 Subchronic Neurotoxicity in Rats (90 days)	Female Adult Week 13	RBC	5.49	4.11
MRID 43608201 Subchronic Neurotoxicity in Rats (90 days)	Male Adult	Brainstem	8.41	6.91
MRID 43608201 Subchronic Neurotoxicity in Rats (90 days)	Female Adult	Brainstem	6.73	5.25
MRID 43608201 Subchronic Neurotoxicity in Rats (90 days)	Female Adult	Hippocampus	No adequate fit	No adequate fit
MRID 432106301 Developmental Rabbit	Female Day 19	RBC	4.94	3.75

[a] Based on visual inspection of graphical outputs, these values are considered adequate.

APPENDIX

MRID 49037404 - Acute CCA Study – Male Adult RBC ChE

Constant Variance - NO

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 ================================================================
        Exponential Model. (Version: 1.9;  Date: 01/29/2013)
        Input Data File: C:/Users/EHOLMAN/Documents/BMDS240/Data/exp_Acute CCA Male
Adult RBC_Setting.(d)
        Gnuplot Plotting File:
                                                Tue Mar 11 15:02:06 2014
 ================================================================

 BMDS Model Run
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   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha          -4.59248          -4.59248           -4.59248          -4.59248
         rho          -2.09382          -2.09382           -2.09382          -2.09382
           a          0.771584          0.898155              1.1571            1.1571
           b        0.00273232      1.52159e-005           0.0144785         0.0144785
           c                --                --               0.536645
0.536645
           d                --                 2                  --                 1
```

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	-4.44419	-4.44419	-4.44475	-4.44475
rho	-1.51542	-1.51542	-1.52347	-1.52347
a	1.07536	1.07536	1.07655	1.07655
b	0.00274706	0.00274706	0.00313867	0.00313871
c	--	--	0.0992428	0.0992505
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	1.102	0.135
15	10	1.017	0.059
30	10	0.96	0.124
90	10	0.863	0.101
180	9	0.652	0.175

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	1.075	0.1026	0.8213
	15	1.032	0.1058	-0.4466
	30	0.9903	0.1092	-0.8772
	90	0.8398	0.1237	0.5928
	180	0.6559	0.1492	-0.0775
3	0	1.075	0.1026	0.8213
	15	1.032	0.1058	-0.4466
	30	0.9903	0.1092	-0.8772
	90	0.8398	0.1237	0.5928
	180	0.6559	0.1492	-0.0775
4	0	1.077	0.1024	0.7856
	15	1.032	0.1058	-0.4471
	30	0.9894	0.1092	-0.8515
	90	0.8379	0.124	0.6398
	180	0.658	0.149	-0.1209
5	0	1.077	0.1024	0.7856
	15	1.032	0.1058	-0.4471
	30	0.9894	0.1092	-0.8515
	90	0.8379	0.124	0.6398
	180	0.658	0.149	-0.1209

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	80.6413	6	-149.2826
A2	85.95203	10	-151.9041
A3	81.89048	7	-149.781
R	56.58668	2	-109.1734
2	80.89807	4	-153.7961
3	80.89807	4	-153.7961
4	80.90056	5	-151.8011
5	80.90056	5	-151.8011

Additive constant for all log-likelihoods = -45.03. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	58.73	8	< 0.0001
Test 2	10.62	4	0.03116
Test 3	8.123	3	0.04354
Test 4	1.985	3	0.5756
Test 5a	1.985	3	0.5756
Test 5b	-1.506e-012	0	N/A
Test 6a	1.98	2	0.3716
Test 6b	0.004976	1	0.9438
Test 7a	1.98	2	0.3716
Test 7b	0.004976	1	0.9438
Test 7c	-6.153e-011	0	N/A

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 4 is greater than .1. Model 2 seems to adequately describe the data.

The p-value for Test 5a is greater than .1. Model 3 seems to adequately describe the data.

Degrees of freedom for Test 5b are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

The p-value for Test 6b is greater than .05. Model 4 does not seem to fit the data better than Model 2.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

The p-value for Test 7b is greater than .05. Model 5 does not seem to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0. The Chi-Square test for fit is not valid.

Benchmark Dose Computations:

Specified Effect = 0.100000

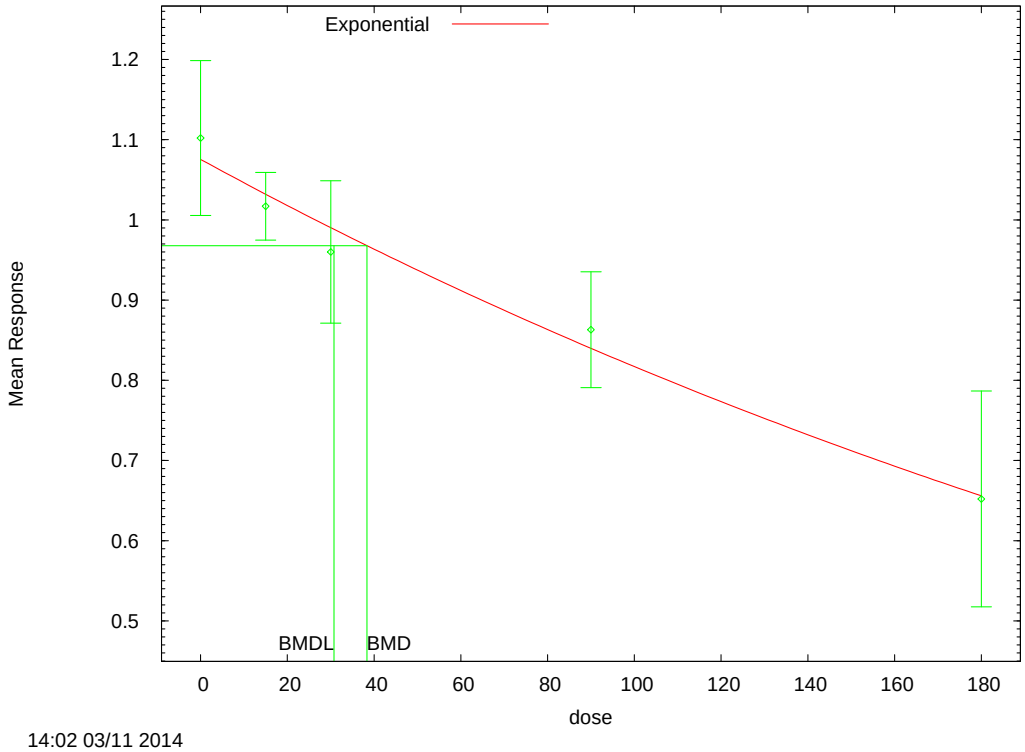
Risk Type = Relative deviation

Confidence Level = 0.950000

BMD and BMDL by Model

Model	BMD	BMDL
2	38.354	30.7598
3	38.354	30.7598
4	37.4929	21.1521
5	37.4928	21.1521

Exponential Model 2, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



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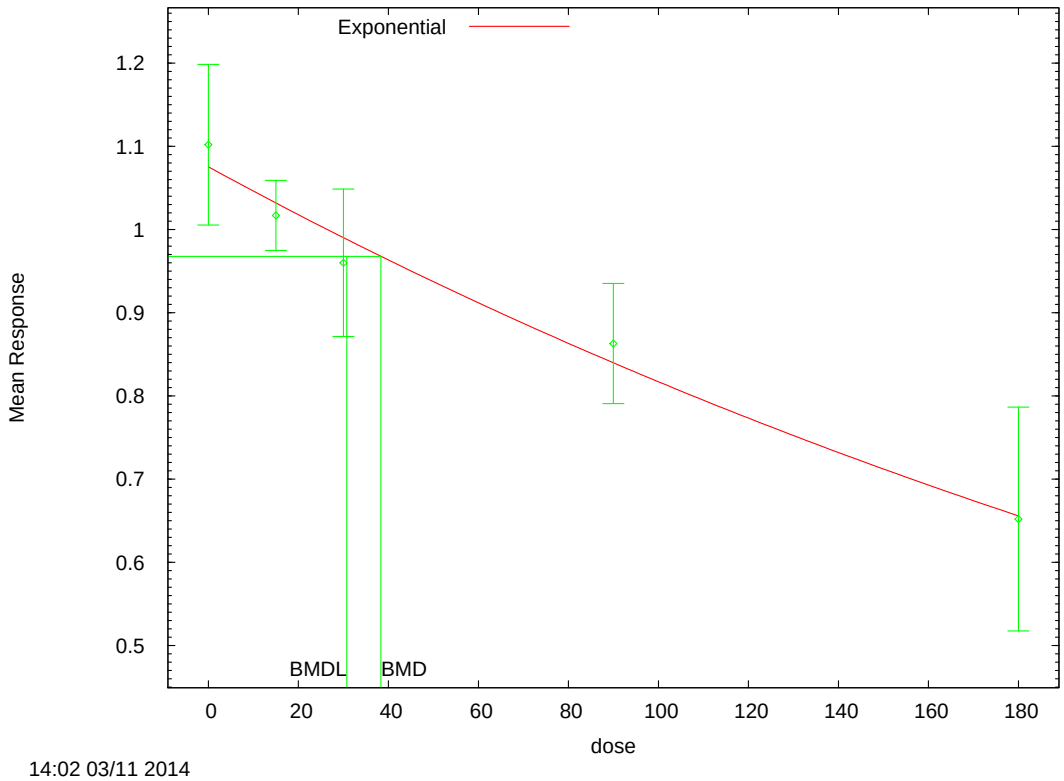
Exponential Model 3, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



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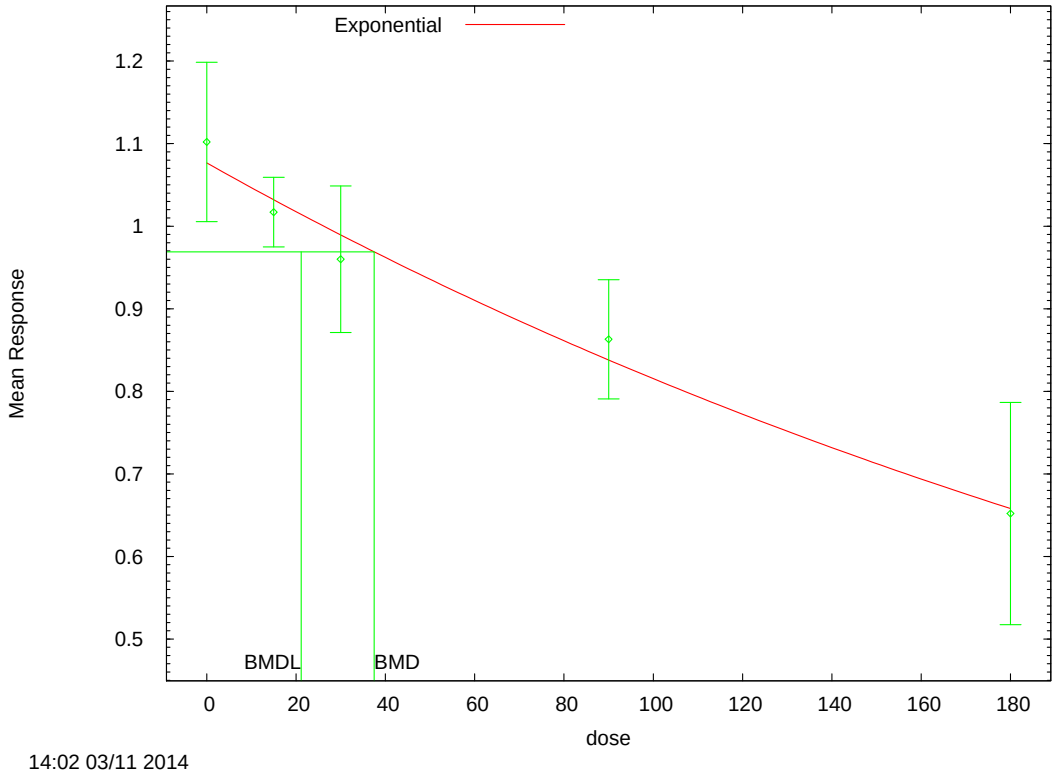
Exponential Model 4, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



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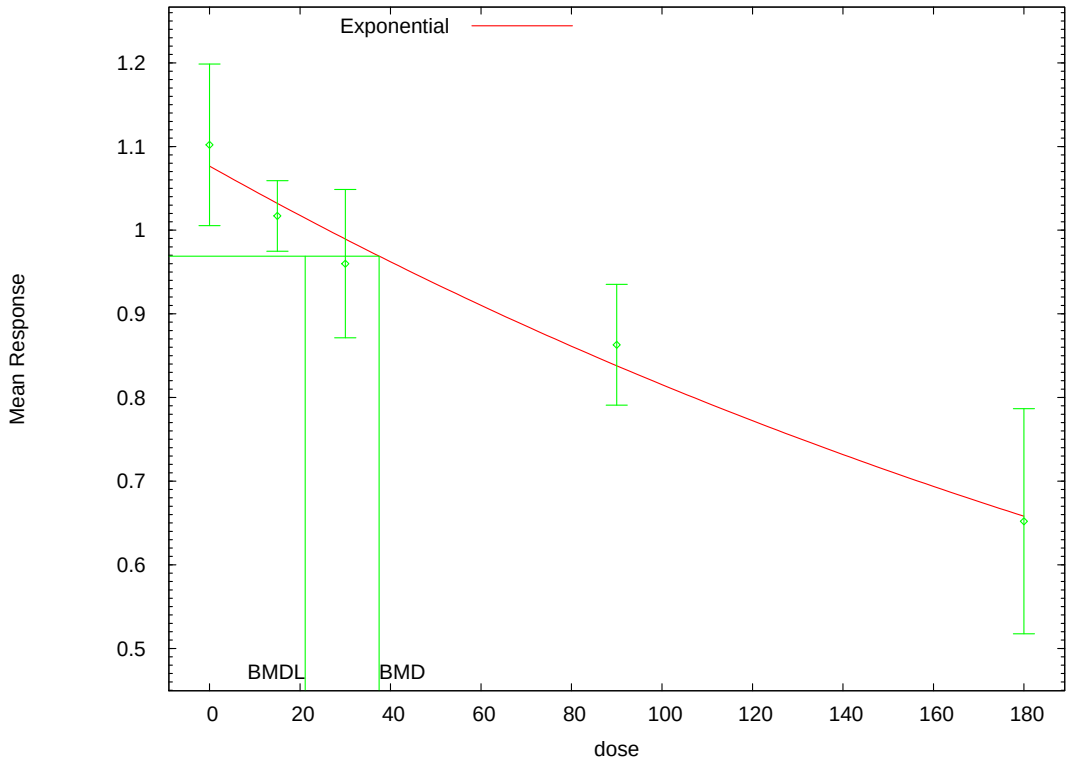
Exponential Model 5, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



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MRID 49037404 - Acute CCA Study – Female Adult RBC ChE

Constant Variance - YES

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        Exponential Model. (Version: 1.9;  Date: 01/29/2013)
        Input Data File: C:/Users/EHOLMAN/Documents/BMDS240/Data/exp_Acute CCA Female
Adult RBC_Setting.(d)
        Gnuplot Plotting File:
                                                Tue Mar 11 15:25:40 2014
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 BMDS Model Run
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   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha          -3.57101          -3.57101           -3.57101          -3.57101
         rho(S)              0                 0                  0                 0
           a          0.766034          0.903343             1.1739            1.1739
           b        0.00327222      1.70208e-005         0.00338485        0.00338485
           c                --                --           0.000541784
0.000541784
           d                --                 2                  --                 1

     (S) = Specified


                              Parameter Estimates by Model
```

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	-3.52115	-3.54505	-3.52115	-3.56896
rho	0	0	0	0
a	1.15207	1.12514	1.15207	1.10574
b	0.00317368	0.00374905	0.00317368	0.0104716
c	--	--	0	0.575182
d	--	1.34806	--	5.16912

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	1.094	0.195
15	10	1.118	0.177
30	10	1.104	0.188
90	10	0.861	0.141
180	10	0.636	0.178

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	1.152	0.1719	-1.068
	15	1.099	0.1719	0.3584
	30	1.047	0.1719	1.04
	90	0.8658	0.1719	-0.08878
	180	0.6507	0.1719	-0.2704
3	0	1.125	0.1699	-0.5795
	15	1.102	0.1699	0.2952
	30	1.068	0.1699	0.6791
	90	0.8929	0.1699	-0.5939
	180	0.6246	0.1699	0.2116
4	0	1.152	0.1719	-1.068
	15	1.099	0.1719	0.3584
	30	1.047	0.1719	1.04
	90	0.8658	0.1719	-0.08878
	180	0.6507	0.1719	-0.2704
5	0	1.106	0.1679	-0.2211
	15	1.106	0.1679	0.2316
	30	1.105	0.1679	-0.01051
	90	0.861	0.1679	2.922e-005
	180	0.636	0.1679	-4.59e-006

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	64.27533	6	-116.5507
A2	64.86043	10	-109.7209
A3	64.27533	6	-116.5507
R	43.79724	2	-83.59448
2	63.02875	3	-120.0575
3	63.62615	4	-119.2523
4	63.02875	3	-120.0575
5	64.22396	5	-118.4479

Additive constant for all log-likelihoods = -45.95. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	42.13	8	< 0.0001
Test 2	1.17	4	0.883
Test 3	1.17	4	0.883
Test 4	2.493	3	0.4765
Test 5a	1.298	2	0.5225
Test 5b	1.195	1	0.2744
Test 6a	2.493	3	0.4765
Test 6b	1.322e-012	0	N/A
Test 7a	0.1027	1	0.7486
Test 7b	1.196	1	0.2742
Test 7c	2.39	2	0.3026

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is greater than .1. A homogeneous variance model appears to be appropriate here.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is greater than .1. Model 2 seems to adequately describe the data.

The p-value for Test 5a is greater than .1. Model 3 seems to adequately describe the data.

The p-value for Test 5b is greater than .05. Model 3 does not seem to fit the data better than Model 2.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

Degrees of freedom for Test 6b are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

The p-value for Test 7b is greater than .05. Model 5 does not seem to fit the data better than Model 3.

The p-value for Test 7c is greater than .05. Model 5 does not seem to fit the data better than Model 4.

Benchmark Dose Computations:

Specified Effect = 0.100000

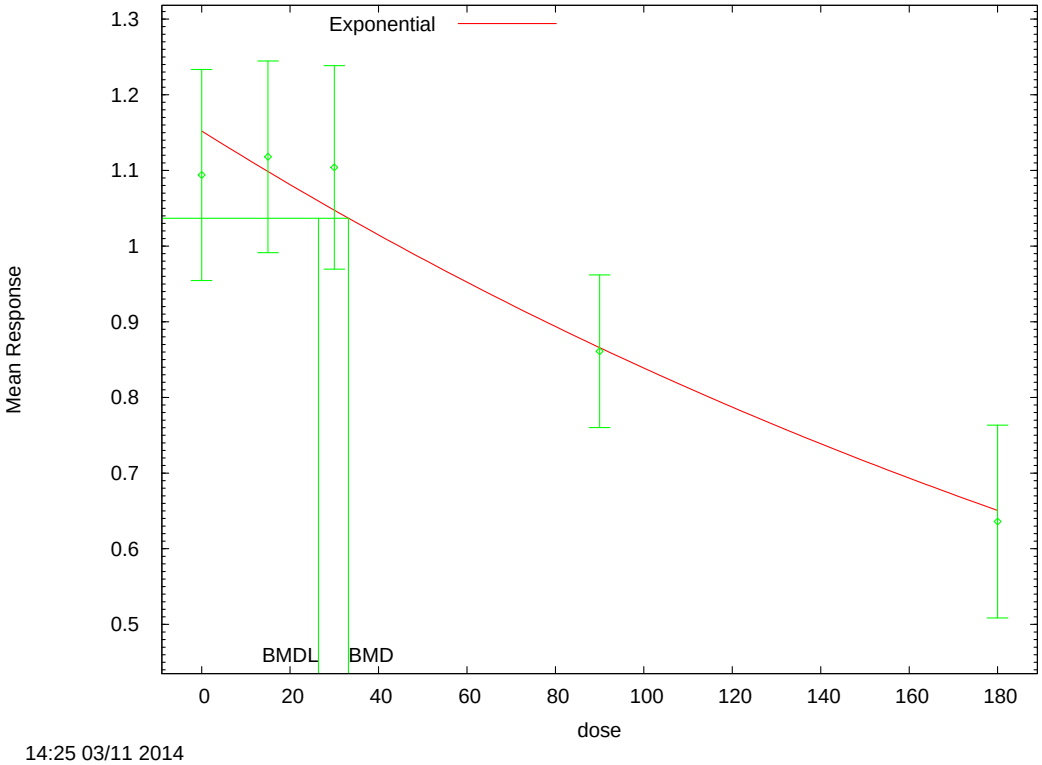
Risk Type = Relative deviation

Confidence Level = 0.950000

BMD and BMDL by Model

Model	BMD	BMDL
2	33.1982	26.4502
3	50.2449	27.9509
4	33.1982	22.5876
5	74.0422	30.3884

Exponential Model 2, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



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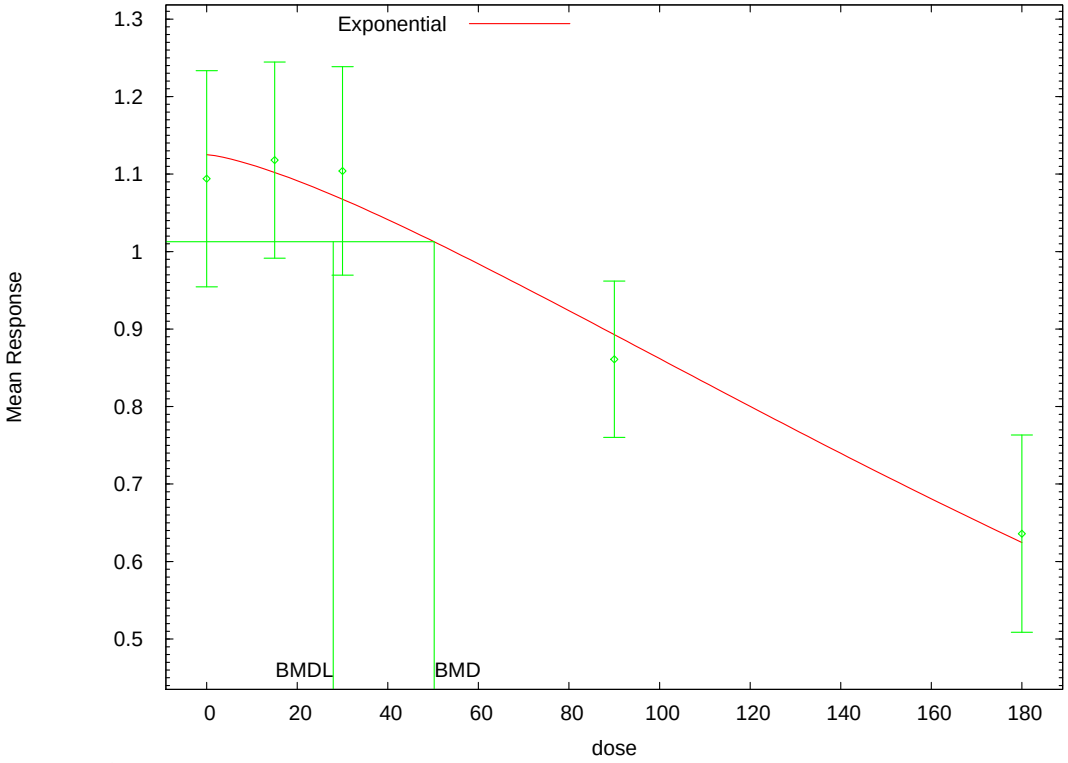
Exponential Model 3, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



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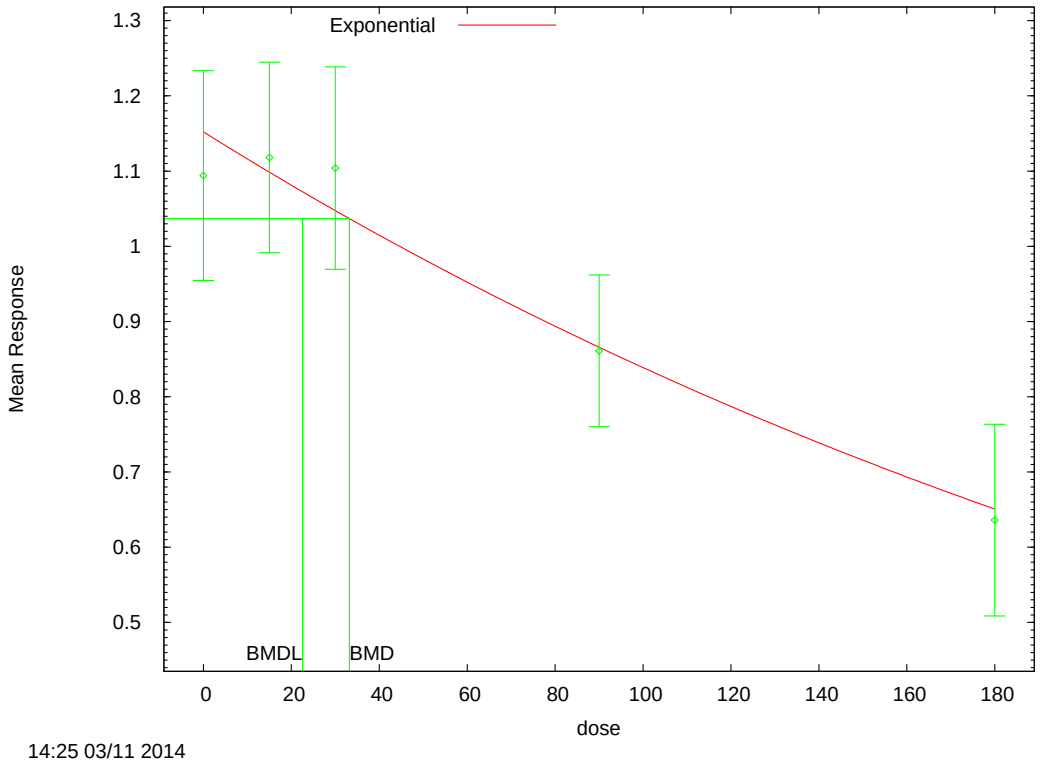
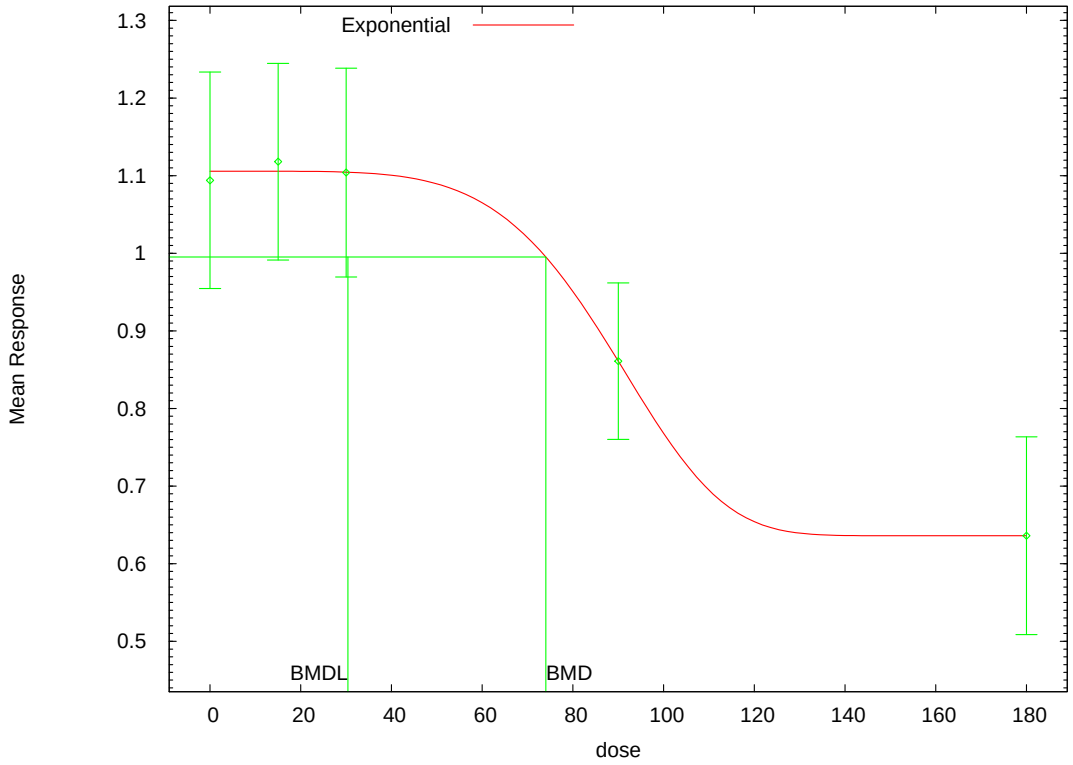
Exponential Model 4, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



14:25 03/11 2014

Exponential Model 5, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



14:25 03/11 2014

```
 ================================================================
        Exponential Model. (Version: 1.9;  Date: 01/29/2013)
        Input Data File: F:/Pirimiphos-methyl/BMD runs/exp_Acute CCA Male Adult
Brain_Setting.(d)
        Gnuplot Plotting File:
                                                Tue Mar 11 16:19:16 2014
 ================================================================

 BMDS Model Run
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   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha           9.31297           9.31297             9.31297           9.31297
         rho          -3.92547          -3.92547            -3.92547          -3.92547
           a            12.508            12.508              14.0511           14.0511
           b       0.000522984       0.000522984          0.00877411        0.00877411
           c                --                --                0.830913
0.830913
           d                --                 1                  --                 1


                               Parameter Estimates by Model

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha        31.3211           31.5877             31.321           31.5877
```

rho	-12.4724	-12.5789	-12.4724	-12.5789
a	13.3899	13.3569	13.3899	13.3569
b	0.000568929	0.000789696	0.000568928	0.0007897
c	--	--	0	1.16253e-020
d	--	1.16229	--	1.1623

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	13.38	0.645
15	10	13.31	0.788
30	10	13.21	0.672
90	10	12.51	0.34
180	10	12.26	1.376

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	13.39	0.595	-0.04194
	15	13.28	0.6275	0.1658
	30	13.16	0.6618	0.2423
	90	12.72	0.8188	-0.8093
	180	12.09	1.127	0.484
3	0	13.36	0.6014	0.1318
	15	13.28	0.6236	0.1464
	30	13.19	0.6522	0.1374
	90	12.75	0.8045	-0.947
	180	12.04	1.154	0.5927
4	0	13.39	0.595	-0.04194
	15	13.28	0.6275	0.1658
	30	13.16	0.6618	0.2423
	90	12.72	0.8188	-0.8093
	180	12.09	1.127	0.484
5	0	13.36	0.6014	0.1318
	15	13.28	0.6236	0.1464
	30	13.19	0.6522	0.1374
	90	12.75	0.8045	-0.947
	180	12.04	1.154	0.5927

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC

A1	-13.43146	6	38.86291
A2	-4.027107	10	28.05421
A3	-10.12105	7	34.24209
R	-20.64835	2	45.2967
2	-10.21386	4	28.42772
3	-10.17053	5	30.34107
4	-10.21386	4	28.42772
5	-10.17053	6	32.34107

Additive constant for all log-likelihoods = -45.95. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	33.24	8	< 0.0001
Test 2	18.81	4	0.000857
Test 3	12.19	3	0.006767
Test 4	0.1856	3	0.9799
Test 5a	0.09897	2	0.9517
Test 5b	0.08665	1	0.7685
Test 6a	0.1856	3	0.9799
Test 6b	-3.226e-012	0	N/A
Test 7a	0.09897	1	0.7531
Test 7b	-1.088e-010	1	N/A
Test 7c	0.08665	2	0.9576

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 4 is greater than .1. Model 2 seems to adequately describe the data.

The p-value for Test 5a is greater than .1. Model 3 seems to adequately describe the data.

The p-value for Test 5b is greater than .05. Model 3 does not seem to fit the data better than Model 2.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

Degrees of freedom for Test 6b are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

The p-value for Test 7b is less than .05. Model 5 appears to fit the data better than Model 3.

The p-value for Test 7c is greater than .05. Model 5 does not seem to fit the data better than Model 4.

Benchmark Dose Computations:

Specified Effect = 0.100000

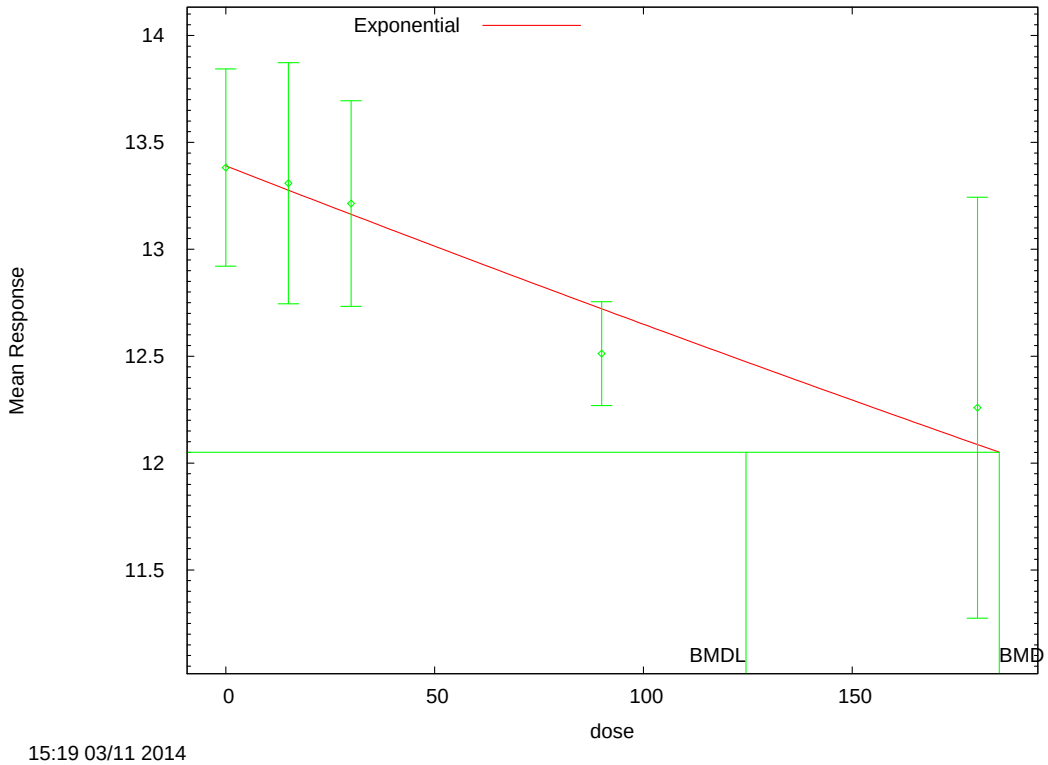
Risk Type = Relative deviation

Confidence Level = 0.950000

BMD and BMDL by Model

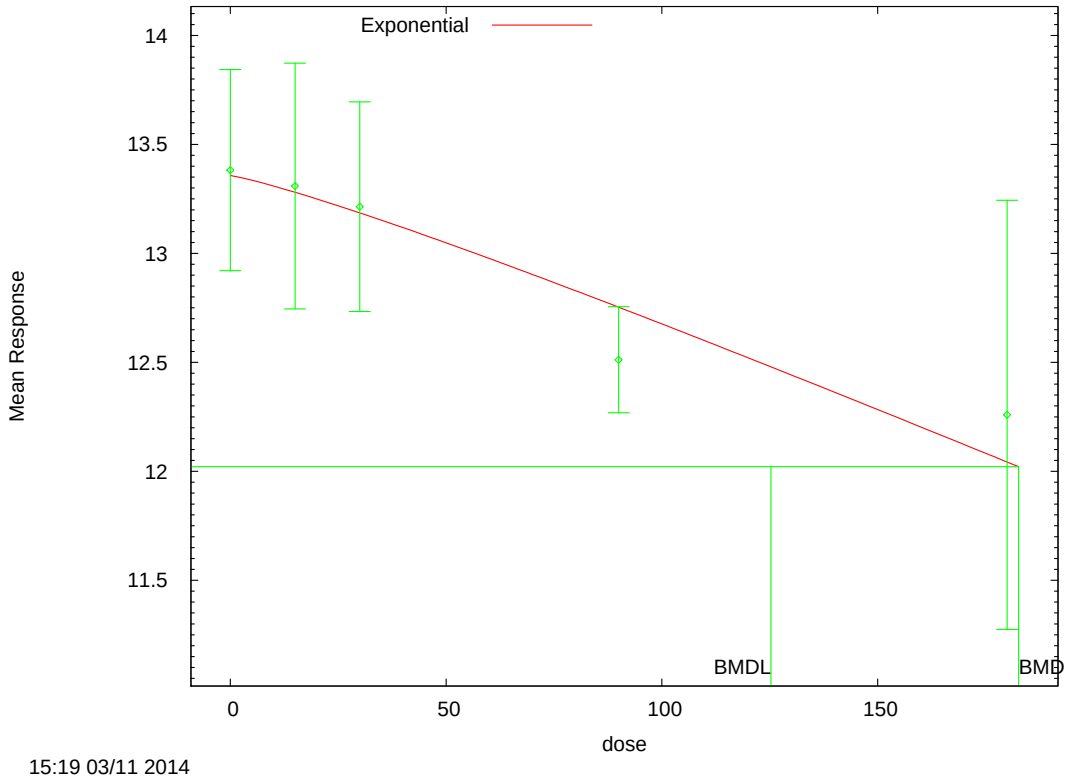
Model	BMD	BMDL
2	185.191	124.576
3	182.677	125.286
4	185.191	121.522
5	182.677	125.286

Exponential Model 2, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



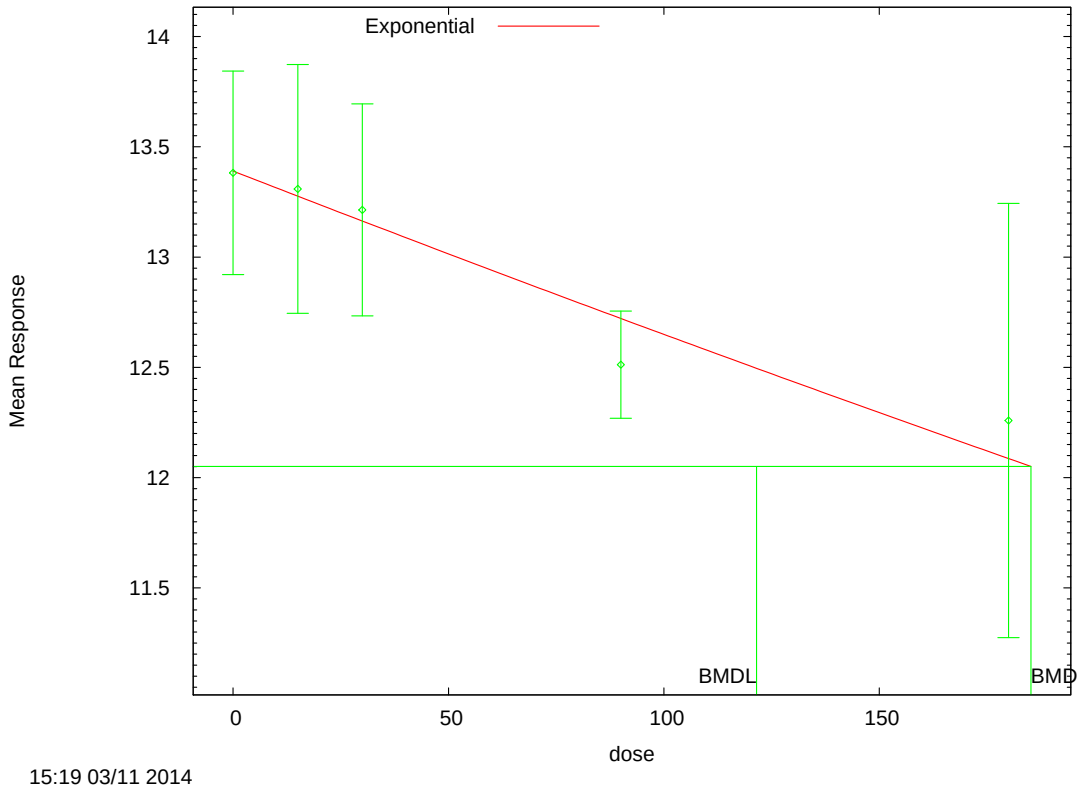
15:19 03/11 2014

Exponential Model 3, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



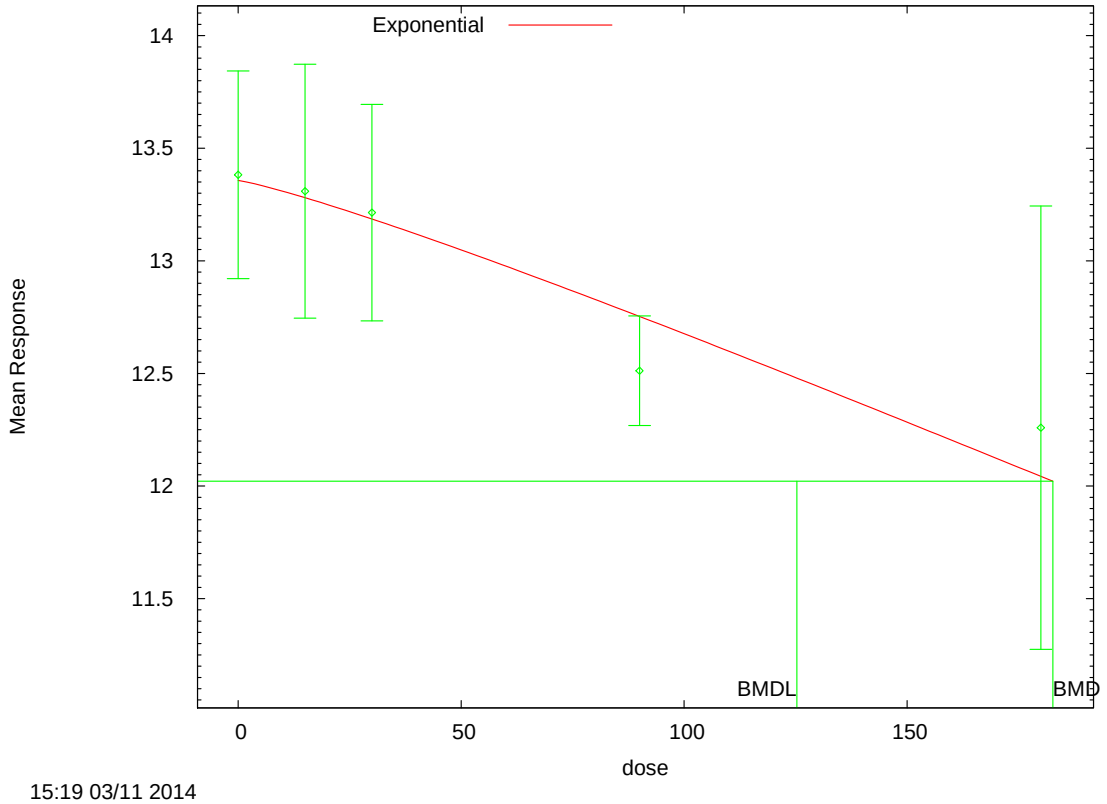
15:19 03/11 2014

Exponential Model 4, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



15:19 03/11 2014

Exponential Model 5, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



15:19 03/11 2014

```
 ================================================================
        Exponential Model. (Version: 1.9;  Date: 01/29/2013)
        Input Data File: F:/Pirimiphos-methyl/BMD runs/exp_Acute CCA Female Adult
Brain_Setting.(d)
        Gnuplot Plotting File:
                                              Tue Mar 11 17:19:46 2014
 ================================================================

 BMDS Model Run
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   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha           18.5732           18.5732             18.5732           18.5732
         rho          -7.85211          -7.85211            -7.85211          -7.85211
           a           11.4695           11.4695             13.2521           13.2521
           b       0.000722493       0.000722493          0.00929562        0.00929562
           c                --                --                0.793768
0.793768
           d                --                 1                  --                 1


                               Parameter Estimates by Model

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
```

lnalpha	13.1672	13.1672	13.6501	13.6501
rho	-5.65702	-5.65701	-5.85196	-5.85196
a	12.57	12.57	12.6013	12.6013
b	0.000733772	0.000733772	0.00339494	0.00339493
c	--	--	0.732669	0.732669
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	12.62	0.362
15	10	12.47	0.746
30	10	12.18	0.762
90	10	11.77	0.507
180	10	11.05	0.912

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	12.57	0.562	0.287
	15	12.43	0.5798	0.1887
	30	12.3	0.5981	-0.5991
	90	11.77	0.6774	0.01544
	180	11.01	0.8166	0.1172
3	0	12.57	0.562	0.287
	15	12.43	0.5798	0.1887
	30	12.3	0.5981	-0.5991
	90	11.77	0.6774	0.01544
	180	11.01	0.8166	0.1172
4	0	12.6	0.555	0.1122
	15	12.43	0.5771	0.1806
	30	12.28	0.5993	-0.486
	90	11.71	0.6871	0.2559
	180	11.06	0.8128	-0.0622
5	0	12.6	0.555	0.1122
	15	12.43	0.5771	0.1806
	30	12.28	0.5993	-0.486
	90	11.71	0.6871	0.2559
	180	11.06	0.8128	-0.0622

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-3.564748	6	19.1295
A2	1.157103	10	17.68579
A3	-2.18397	7	18.36794
R	-17.62033	2	39.24065
2	-2.726217	4	13.45243
3	-2.726217	4	13.45243
4	-2.66946	5	15.33892
5	-2.66946	5	15.33892

Additive constant for all log-likelihoods = -45.95. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	37.55	8	< 0.0001
Test 2	9.444	4	0.05092
Test 3	6.682	3	0.08275
Test 4	1.084	3	0.7808
Test 5a	1.084	3	0.7808
Test 5b	6.934e-012	0	N/A
Test 6a	0.971	2	0.6154
Test 6b	0.1135	1	0.7362
Test 7a	0.971	2	0.6154
Test 7b	0.1135	1	0.7362
Test 7c	7.612e-013	0	N/A

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 4 is greater than .1. Model 2 seems

to adequately describe the data.

The p-value for Test 5a is greater than .1. Model 3 seems to adequately describe the data.

Degrees of freedom for Test 5b are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

The p-value for Test 6b is greater than .05. Model 4 does not seem to fit the data better than Model 2.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

The p-value for Test 7b is greater than .05. Model 5 does not seem to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0. The Chi-Square test for fit is not valid.

Benchmark Dose Computations:

Specified Effect = 0.100000

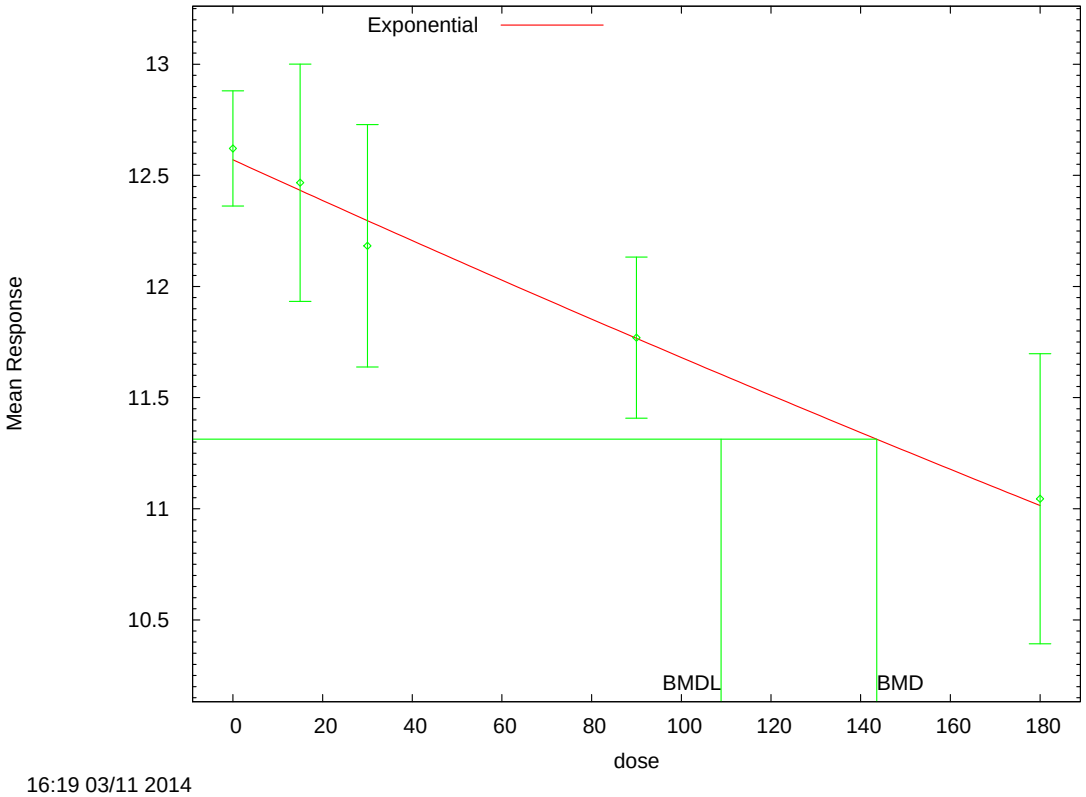
Risk Type = Relative deviation

Confidence Level = 0.950000

BMD and BMDL by Model

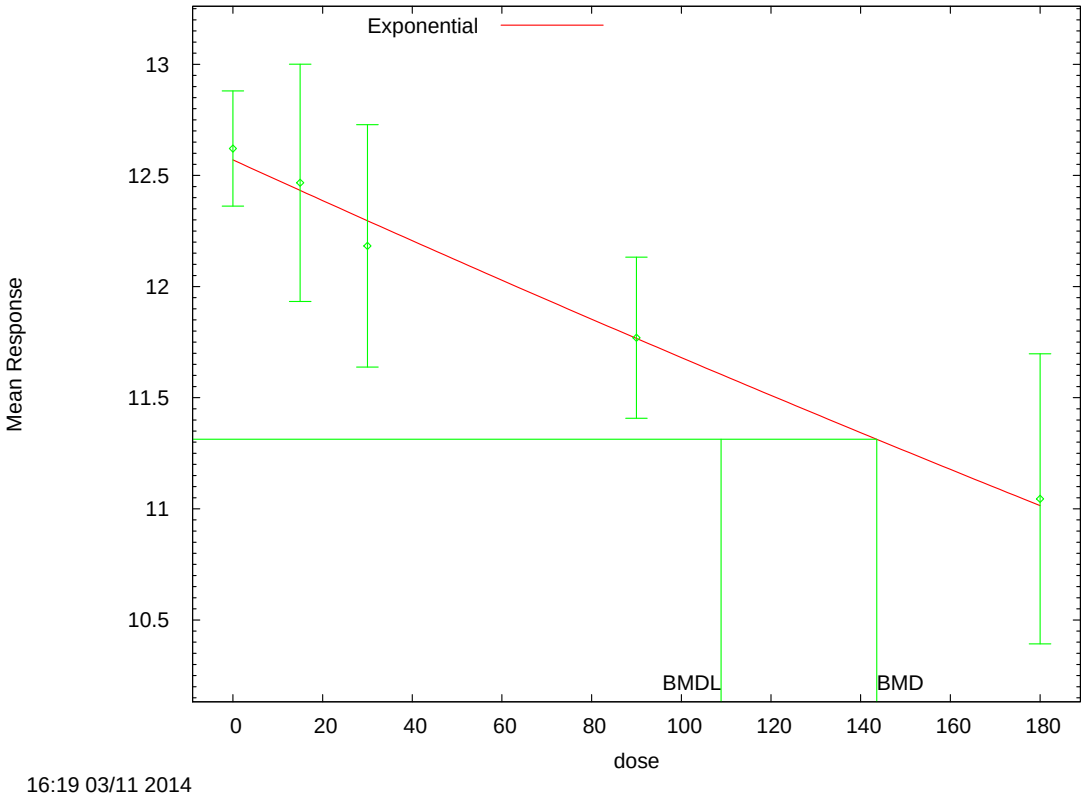
Model	BMD	BMDL
2	143.588	108.856
3	143.588	108.856
4	138.004	80.7849
5	138.004	80.7849

Exponential Model 2, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



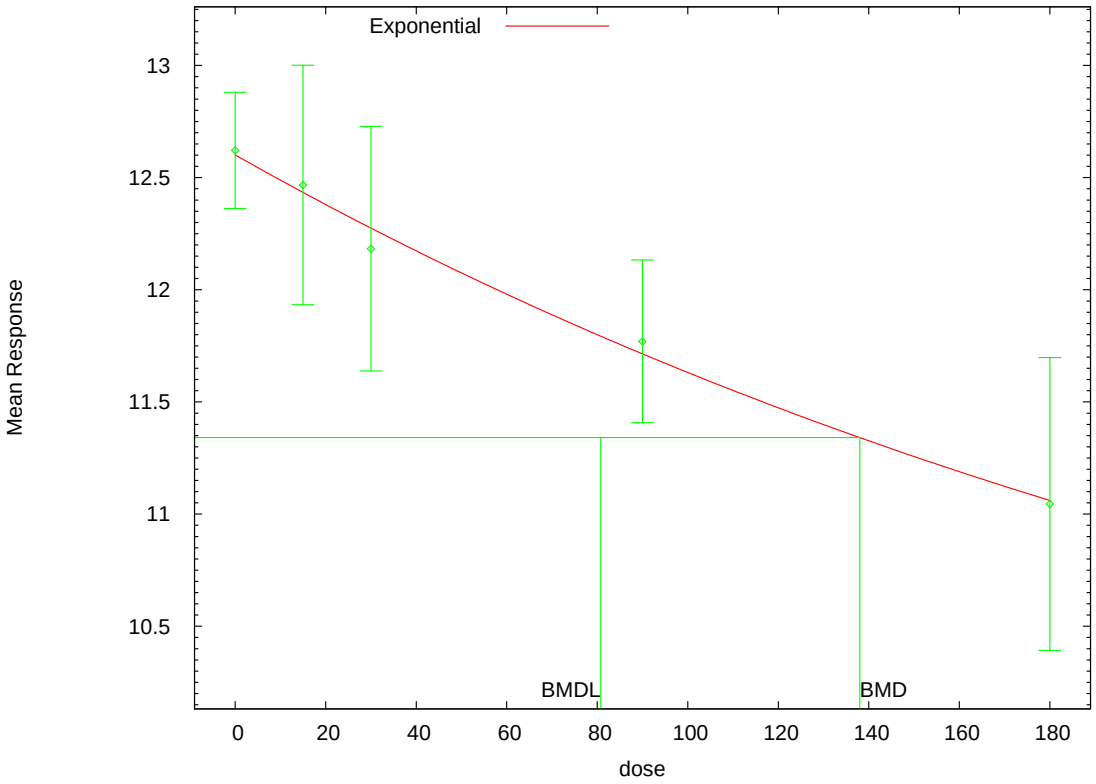
16:19 03/11 2014

Exponential Model 3, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



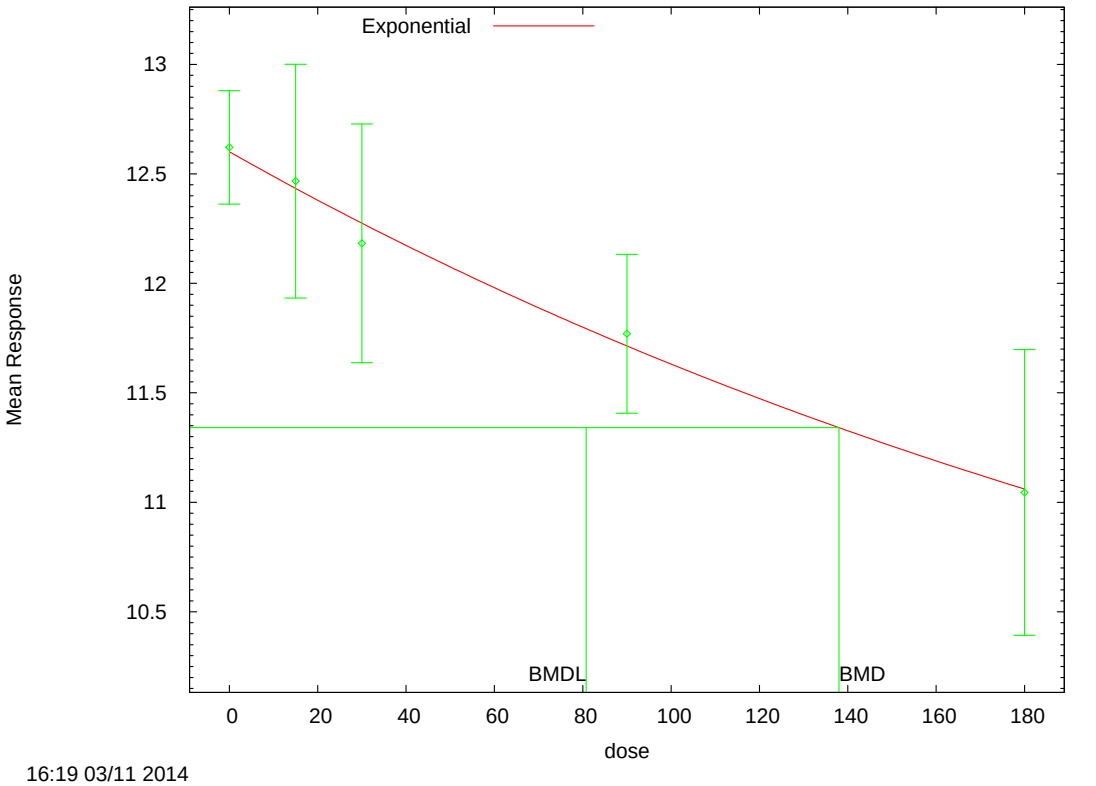
16:19 03/11 2014

Exponential Model 4, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



16:19 03/11 2014

Exponential Model 5, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



16:19 03/11 2014

MRID 49037404 - Acute CCA Study – Male Pup RBC ChE PND12 – Non-Constant Variance

```
 ================================================================
        Exponential Model. (Version: 1.9;  Date: 01/29/2013)
        Input Data File: F:/Pirimiphos-methyl/BMD runs/exp_Acute CCA Male Pup PND12
RBC_Setting.(d)
        Gnuplot Plotting File:
                                                Tue Apr 01 10:21:22 2014
 ================================================================

 BMDS Model Run
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   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha          -2.88703          -2.88703           -2.88703          -2.88703
         rho           0.69329           0.69329            0.69329           0.69329
           a          0.554162          0.838702               1.869             1.869
           b         0.0142609       0.000124011           0.0214286         0.0214286
           c                --                --               0.136437
0.136437
           d                --                 2                     --                 1


                               Parameter Estimates by Model

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha       -2.72499          -2.72499             -2.7404          -2.74546
```

rho	0.705328	0.705328	0.74511	0.809457
a	1.74634	1.74634	1.78194	1.75567
b	0.0149144	0.0149144	0.0198666	0.0245287
c	--	--	0.126183	0.230757
d	--	1	--	1.25776

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	1.78	0.26
15	9	1.374	0.201
30	10	1.113	0.434
60	10	0.651	0.167
90	10	0.51	0.187

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	1.746	0.3116	0.3415
	15	1.396	0.288	-0.232
	30	1.116	0.2662	-0.04015
	60	0.7137	0.2273	-0.8718
	90	0.4562	0.1941	0.876
3	0	1.746	0.3116	0.3415
	15	1.396	0.288	-0.232
	30	1.116	0.2662	-0.04015
	60	0.7137	0.2273	-0.8718
	90	0.4562	0.1941	0.876
4	0	1.782	0.3151	-0.01948
	15	1.381	0.2865	-0.06997
	30	1.083	0.2617	0.3646
	60	0.6976	0.2222	-0.6634
	90	0.4853	0.1941	0.4017
5	0	1.756	0.3182	0.2418
	15	1.421	0.2922	-0.4869
	30	1.089	0.2623	0.2846
	60	0.6708	0.2156	-0.2909
	90	0.4952	0.1907	0.2452

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC

A1	42.40963	6	-72.81926
A2	49.05921	10	-78.11843
A3	43.95549	7	-73.91099
R	6.243927	2	-8.487854
2	42.80566	4	-77.61132
3	42.80566	4	-77.61132
4	43.14426	5	-76.28852
5	43.3184	6	-74.63679

Additive constant for all log-likelihoods = -45.03. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	85.63	8	< 0.0001
Test 2	13.3	4	0.009903
Test 3	10.21	3	0.01688
Test 4	2.3	3	0.5126
Test 5a	2.3	3	0.5126
Test 5b	-2.174e-012	0	N/A
Test 6a	1.622	2	0.4443
Test 6b	0.6772	1	0.4106
Test 7a	1.274	1	0.259
Test 7b	1.025	2	0.5989
Test 7c	0.3483	1	0.5551

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 4 is greater than .1. Model 2 seems to adequately describe the data.

The p-value for Test 5a is greater than .1. Model 3 seems to adequately describe the data.

Degrees of freedom for Test 5b are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

The p-value for Test 6b is greater than .05. Model 4 does not seem to fit the data better than Model 2.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

The p-value for Test 7b is greater than .05. Model 5 does not seem to fit the data better than Model 3.

The p-value for Test 7c is greater than .05. Model 5 does not seem to fit the data better than Model 4.

Benchmark Dose Computations:

Specified Effect = 0.100000

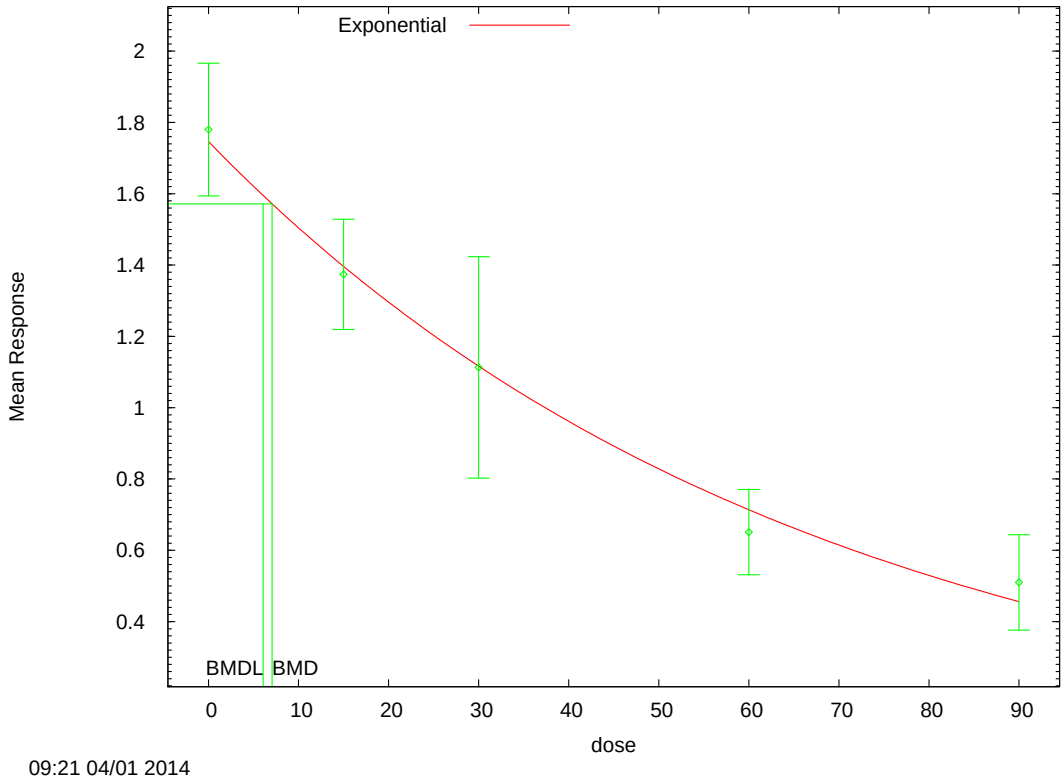
Risk Type = Relative deviation

Confidence Level = 0.950000

BMD and BMDL by Model

Model	BMD	BMDL
2	7.06436	6.07204
3	7.06436	6.07204
4	6.11759	4.54205
5	8.5038	4.63079

Exponential Model 2, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



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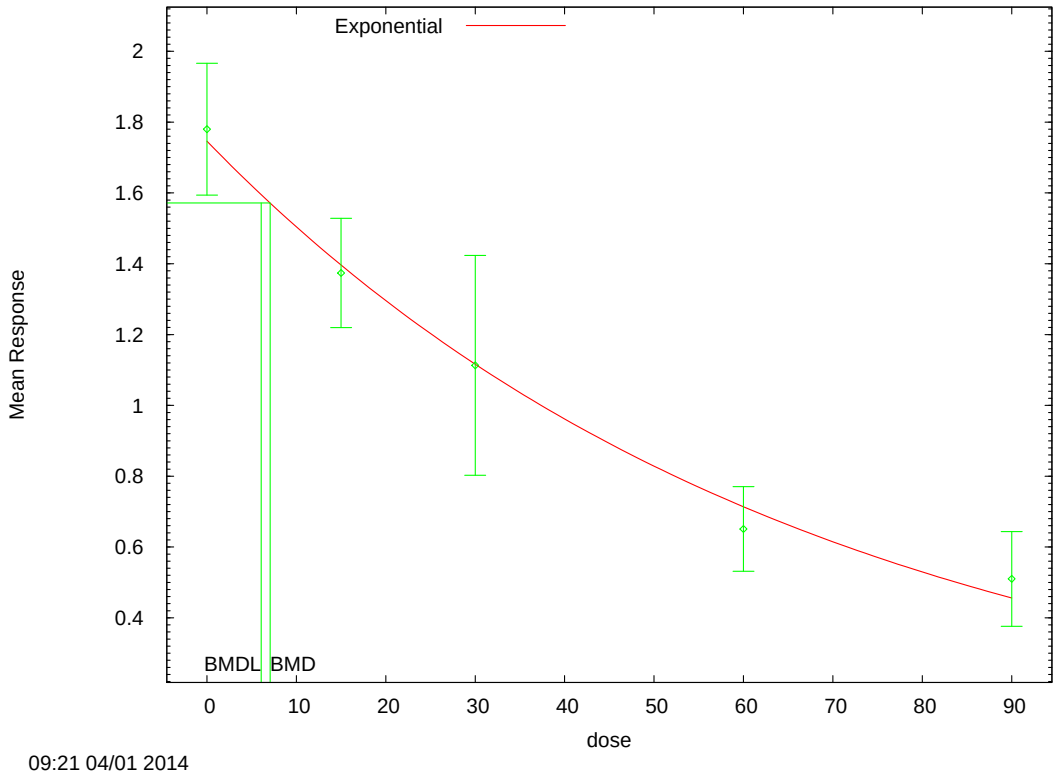
Exponential Model 3, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



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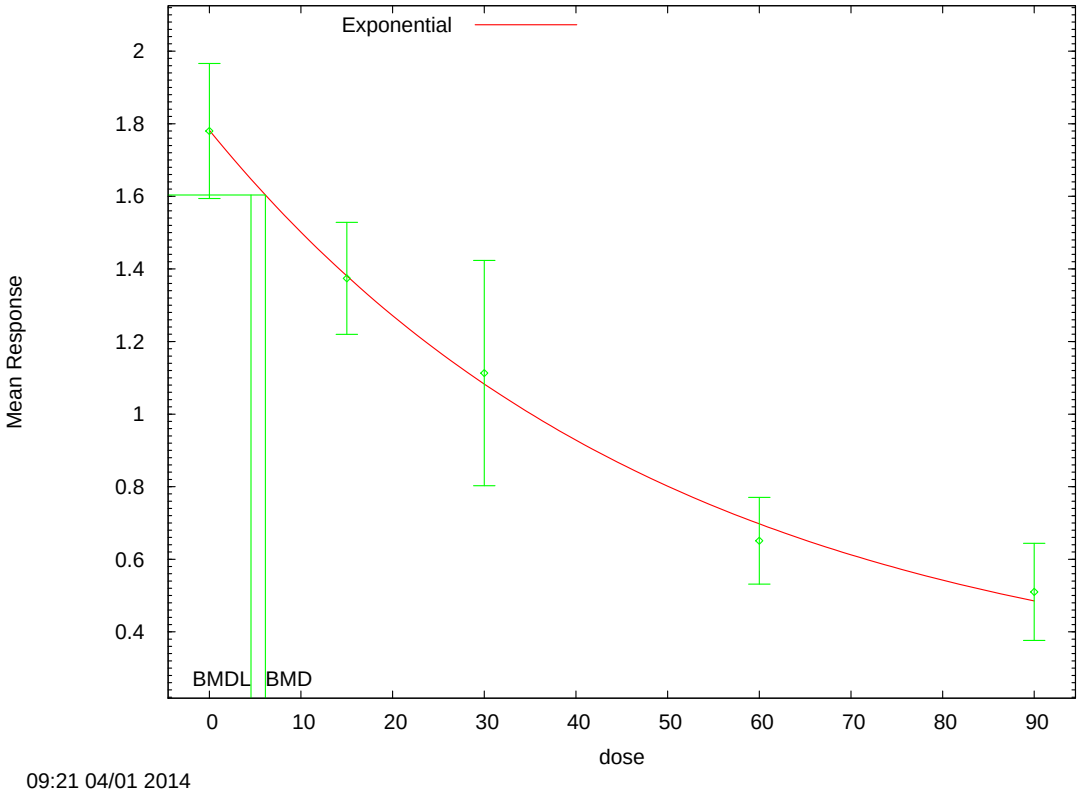
Exponential Model 4, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



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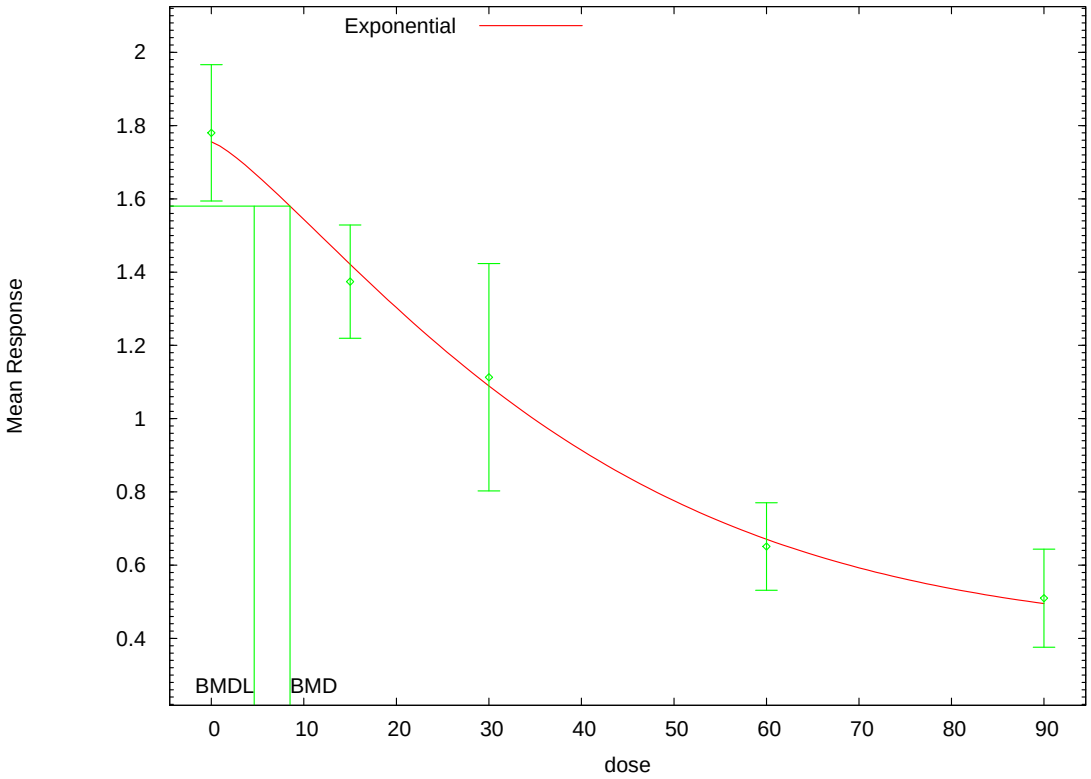
Exponential Model 5, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



09:21 04/01 2014

MRID 49037404 - Acute CCA Study – Female Pup RBC ChE PND12 – Non-Constant Variance

```
 ================================================================
        Exponential Model. (Version: 1.9;  Date: 01/29/2013)
        Input Data File: F:/Pirimiphos-methyl/BMD runs/exp_Acute CCA Female Pup PND12
RBC_Setting.(d)
        Gnuplot Plotting File:
                                                Tue Apr 01 10:39:35 2014
 ================================================================

 BMDS Model Run
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   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha          -3.43397          -3.43397           -3.43397          -3.43397
         rho           1.88229           1.88229            1.88229           1.88229
           a          0.610896          0.880025            1.84905           1.84905
           b         0.0135383       0.000113602           0.0198113         0.0198113
           c                --                --               0.145751
0.145751
           d                --                 2                    --                 1


                               Parameter Estimates by Model

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha       -3.41504          -3.41504           -3.42304          -3.44167
```

rho	1.88629	1.88629	1.93138	1.98505
a	1.75835	1.75835	1.78605	1.7353
b	0.013538	0.013538	0.0161498	0.0216832
c	--	--	0.0808937	0.246025
d	--	1	--	1.37076

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	1.761	0.361
15	10	1.404	0.186
30	10	1.246	0.238
60	10	0.718	0.138
90	10	0.539	0.1

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	1.758	0.3087	0.02712
	15	1.435	0.2549	-0.3871
	30	1.171	0.2105	1.12
	60	0.7804	0.1435	-1.376
	90	0.5199	0.09784	0.616
3	0	1.758	0.3087	0.02712
	15	1.435	0.2549	-0.3871
	30	1.171	0.2105	1.12
	60	0.7804	0.1435	-1.376
	90	0.5199	0.09784	0.616
4	0	1.786	0.3162	-0.2505
	15	1.433	0.2556	-0.3574
	30	1.156	0.2077	1.375
	60	0.7674	0.1399	-1.117
	90	0.5282	0.0975	0.3501
5	0	1.735	0.3092	0.2629
	15	1.483	0.2645	-0.9414
	30	1.178	0.2106	1.017
	60	0.7387	0.1325	-0.4938
	90	0.5343	0.09604	0.1557

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC

A1	52.46689	6	-92.93379
A2	61.82859	10	-103.6572
A3	60.84161	7	-107.6832
R	10.03626	2	-16.07252
2	58.65954	4	-109.3191
3	58.65954	4	-109.3191
4	58.82424	5	-107.6485
5	59.26092	6	-106.5218

Additive constant for all log-likelihoods = -45.95. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	103.6	8	< 0.0001
Test 2	18.72	4	0.0008906
Test 3	1.974	3	0.5778
Test 4	4.364	3	0.2247
Test 5a	4.364	3	0.2247
Test 5b	1.648e-012	0	N/A
Test 6a	4.035	2	0.133
Test 6b	0.3294	1	0.566
Test 7a	3.161	1	0.0754
Test 7b	1.203	2	0.5481
Test 7c	0.8734	1	0.35

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is greater than .1. Model 2 seems to adequately describe the data.

The p-value for Test 5a is greater than .1. Model 3 seems
to adequately describe the data.

Degrees of freedom for Test 5b are less than or equal to 0.
The Chi-Square test for fit is not valid.

The p-value for Test 6a is greater than .1. Model 4 seems
to adequately describe the data.

The p-value for Test 6b is greater than .05. Model 4 does
not seem to fit the data better than Model 2.

The p-value for Test 7a is less than .1. Model 5 may not adequately
describe the data; you may want to consider another model.

The p-value for Test 7b is greater than .05. Model 5 does
not seem to fit the data better than Model 3.

The p-value for Test 7c is greater than .05. Model 5 does
not seem to fit the data better than Model 4.

Benchmark Dose Computations:

Specified Effect = 0.100000

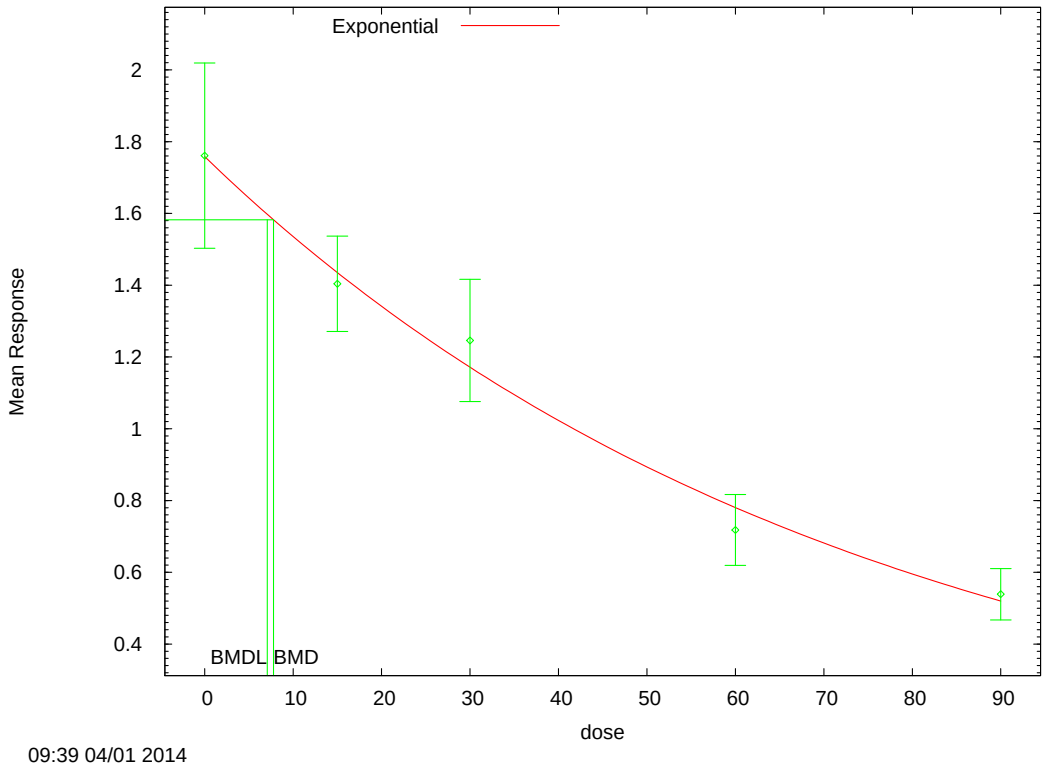
Risk Type = Relative deviation

Confidence Level = 0.950000

BMD and BMDL by Model

Model	BMD	BMDL
2	7.78259	7.06688
3	7.7826	7.06688
4	7.13246	5.54379
5	11.1199	5.79115

Exponential Model 2, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



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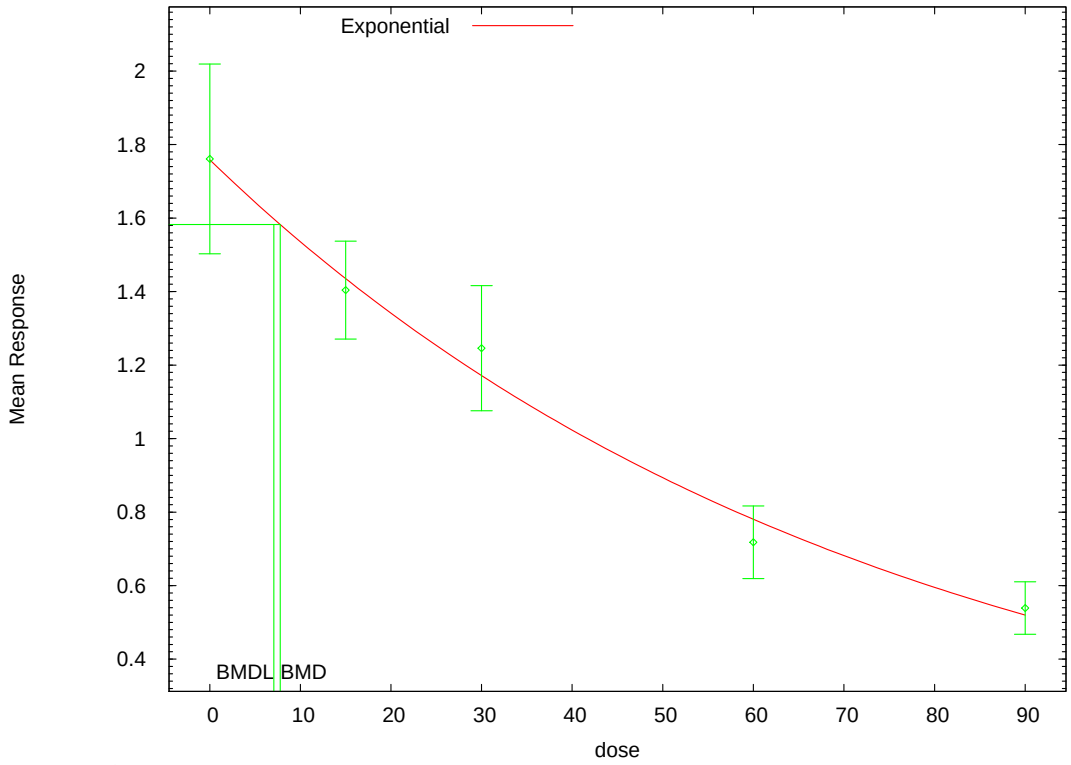
Exponential Model 3, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



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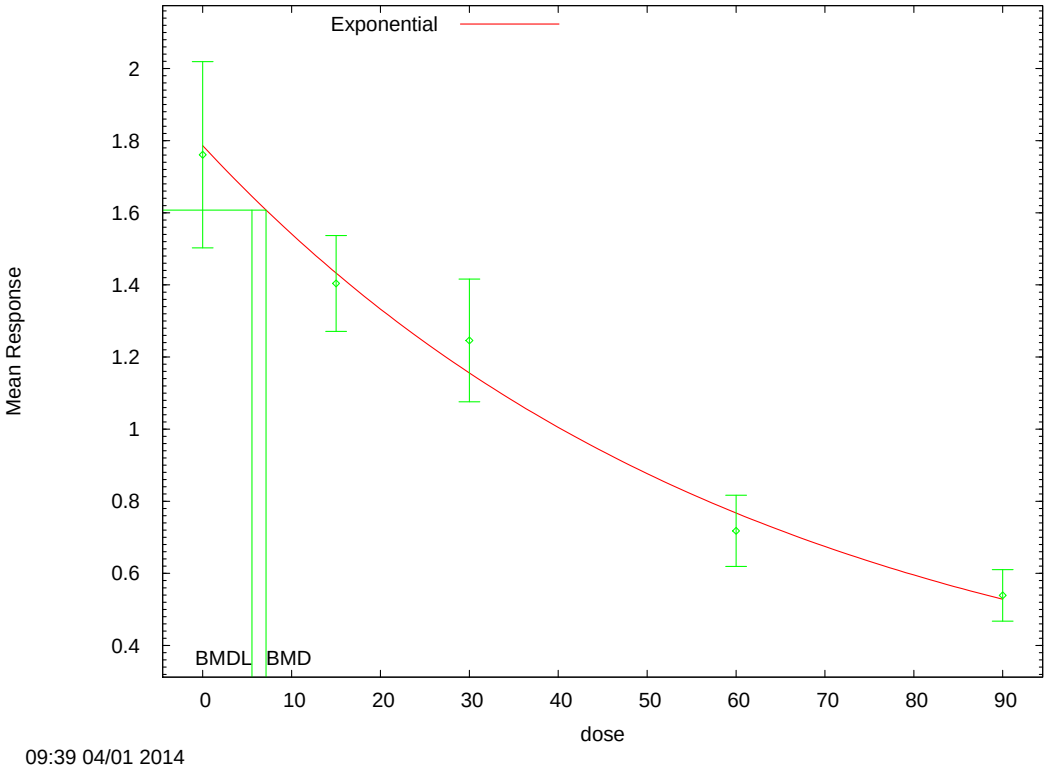
Exponential Model 4, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



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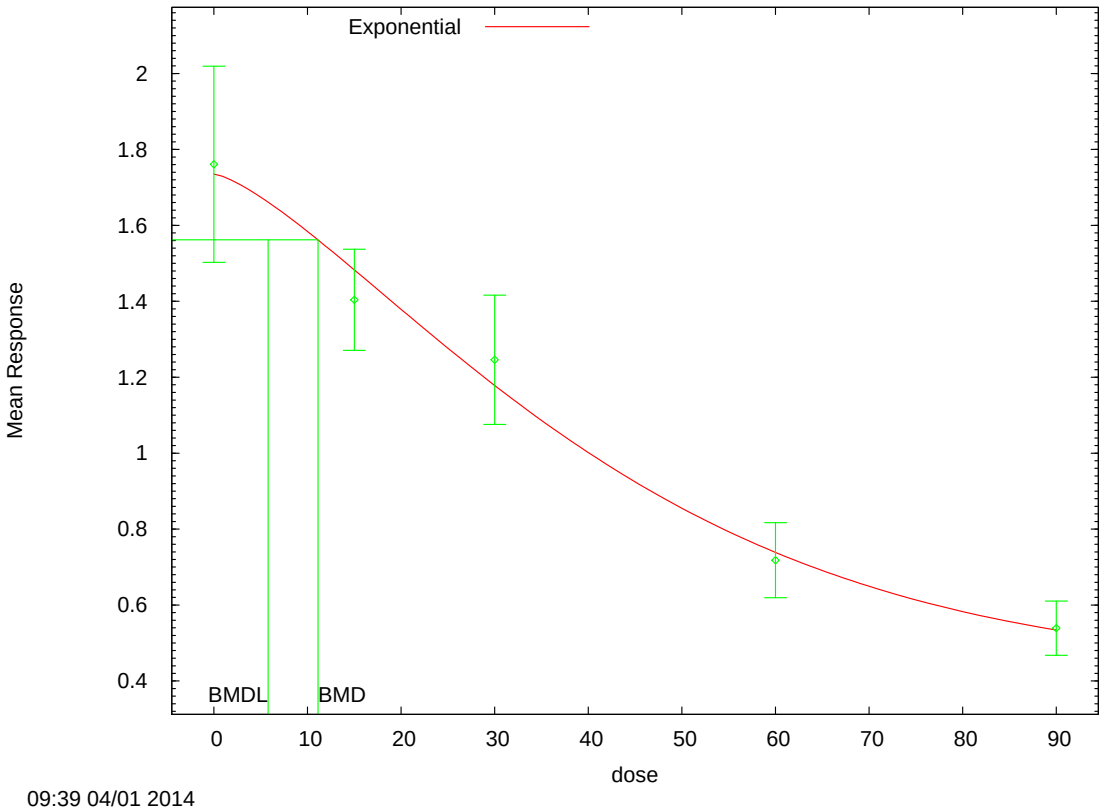
Exponential Model 5, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



09:39 04/01 2014

MRID 49037404 - Acute CCA Study – Male Pup Brain ChE PND12 –Non-Constant Variance

```
 ================================================================
        Exponential Model. (Version: 1.9;  Date: 01/29/2013)
        Input Data File: F:/Pirimiphos-methyl/BMD runs/exp_Acute CCA Male Pup PND12
Brain_Setting.(d)
        Gnuplot Plotting File:
                                                Tue Apr 01 11:00:55 2014
 ================================================================

 BMDS Model Run
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   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha           3.05888           3.05888             3.05888           3.05888
         rho          -3.25857          -3.25857            -3.25857          -3.25857
           a           3.54185           2.56767             6.78615           6.78615
           b        0.00731216      -0.000118941           0.0311654         0.0311654
           c                --                --                0.465233
0.465233
           d                --                 2                  --                 1


                               Parameter Estimates by Model

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
```

lnalpha	2.22905	2.22905	3.01762	3.08284
rho	-2.65145	-2.65146	-3.20313	-3.24517
a	6.39346	6.39346	6.46896	6.46633
b	0.00819114	0.00819115	0.0176943	0.0195024
c	--	--	0.402511	0.432723
d	--	1	--	1.04365

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.463	0.223
15	10	5.581	0.197
30	10	4.874	0.54
60	10	3.98	0.511
90	10	3.315	0.568

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	6.393	0.2605	0.8441
	15	5.654	0.3066	-0.7555
	30	5.001	0.3609	-1.109
	60	3.911	0.4998	0.4362
	90	3.059	0.6923	1.17
3	0	6.393	0.2605	0.8441
	15	5.654	0.3066	-0.7555
	30	5.001	0.3609	-1.109
	60	3.911	0.4998	0.4362
	90	3.059	0.6923	1.17
4	0	6.469	0.2273	-0.08293
	15	5.568	0.2891	0.1427
	30	4.877	0.3574	-0.02639
	60	3.941	0.5028	0.2471
	90	3.39	0.6399	-0.371
5	0	6.466	0.226	-0.04665
	15	5.578	0.2872	0.03167
	30	4.869	0.358	0.04064
	60	3.927	0.5075	0.3282
	90	3.405	0.6397	-0.4458

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	18.78959	6	-25.57919
A2	27.41742	10	-34.83484
A3	24.03064	7	-34.06128
R	-33.82639	2	71.65278
2	21.07762	4	-34.15524
3	21.07762	4	-34.15524
4	23.85364	5	-37.70728
5	23.86898	6	-35.73796

Additive constant for all log-likelihoods = -45.95. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	122.5	8	< 0.0001
Test 2	17.26	4	0.001724
Test 3	6.774	3	0.07948
Test 4	5.906	3	0.1163
Test 5a	5.906	3	0.1163
Test 5b	-3.172e-011	0	N/A
Test 6a	0.354	2	0.8378
Test 6b	5.552	1	0.01846
Test 7a	0.3233	1	0.5696
Test 7b	5.583	2	0.06134
Test 7c	0.03067	1	0.861

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 4 is greater than .1. Model 2 seems

to adequately describe the data.

The p-value for Test 5a is greater than .1. Model 3 seems to adequately describe the data.

Degrees of freedom for Test 5b are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

The p-value for Test 6b is less than .05. Model 4 appears to fit the data better than Model 2.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

The p-value for Test 7b is greater than .05. Model 5 does not seem to fit the data better than Model 3.

The p-value for Test 7c is greater than .05. Model 5 does not seem to fit the data better than Model 4.

Benchmark Dose Computations:

Specified Effect = 0.100000

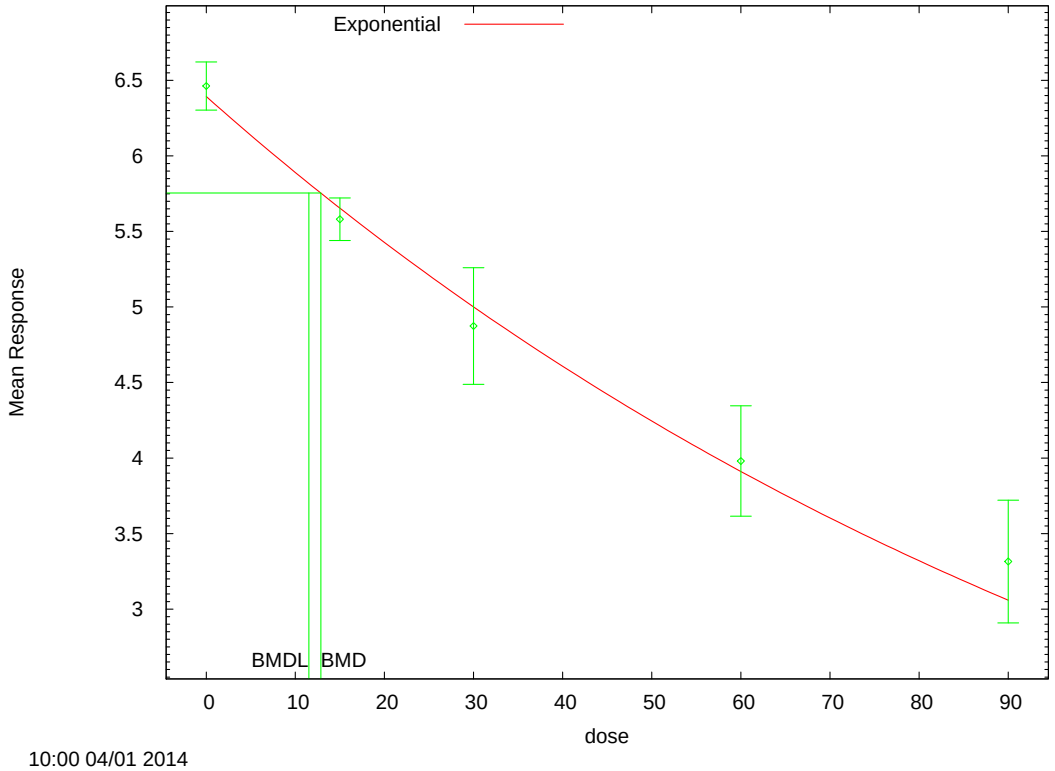
Risk Type = Relative deviation

Confidence Level = 0.950000

BMD and BMDL by Model

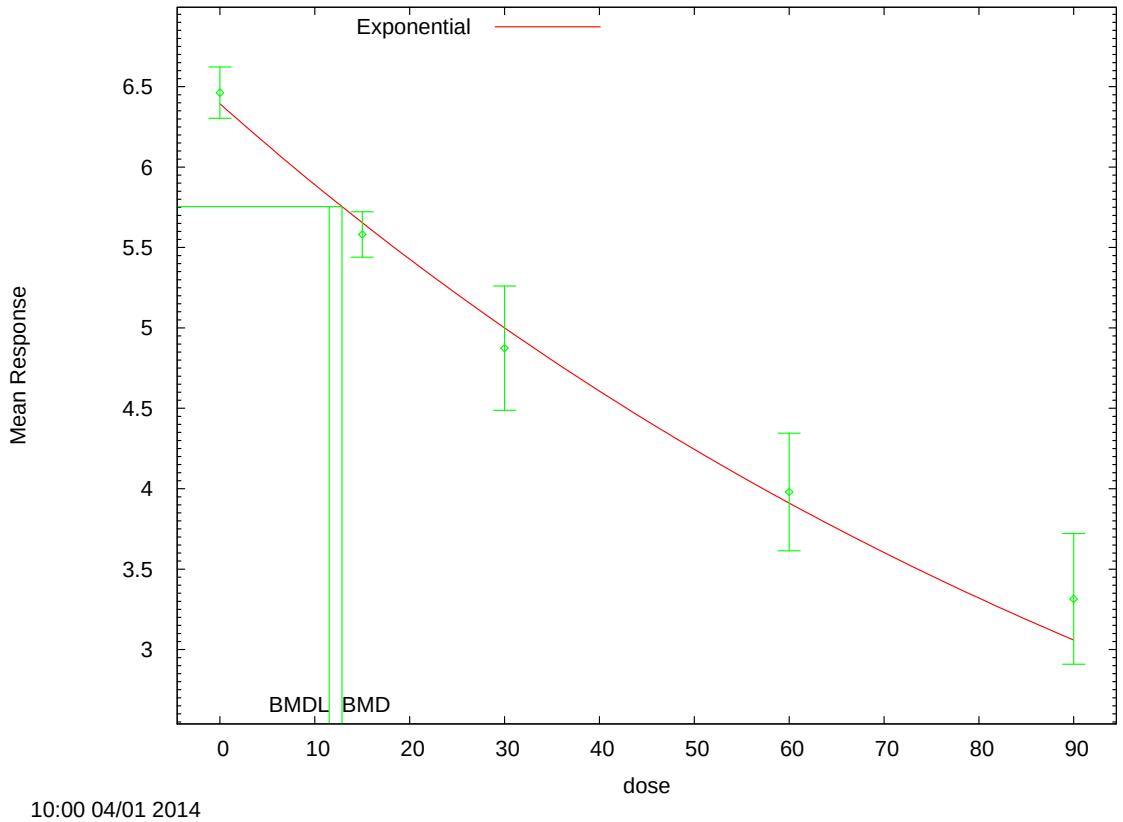
Model	BMD	BMDL
2	12.8627	11.5169
3	12.8627	11.5169
4	10.3515	8.77425
5	10.6498	8.7826

Exponential Model 2, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



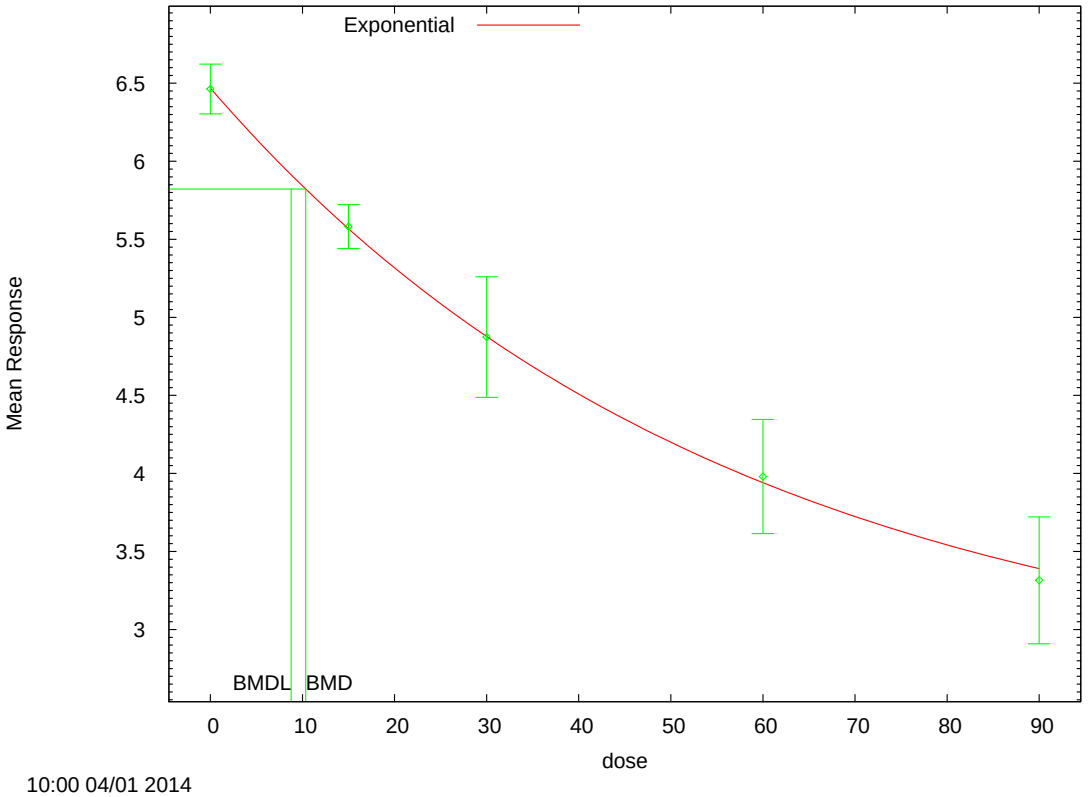
10:00 04/01 2014

Exponential Model 3, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



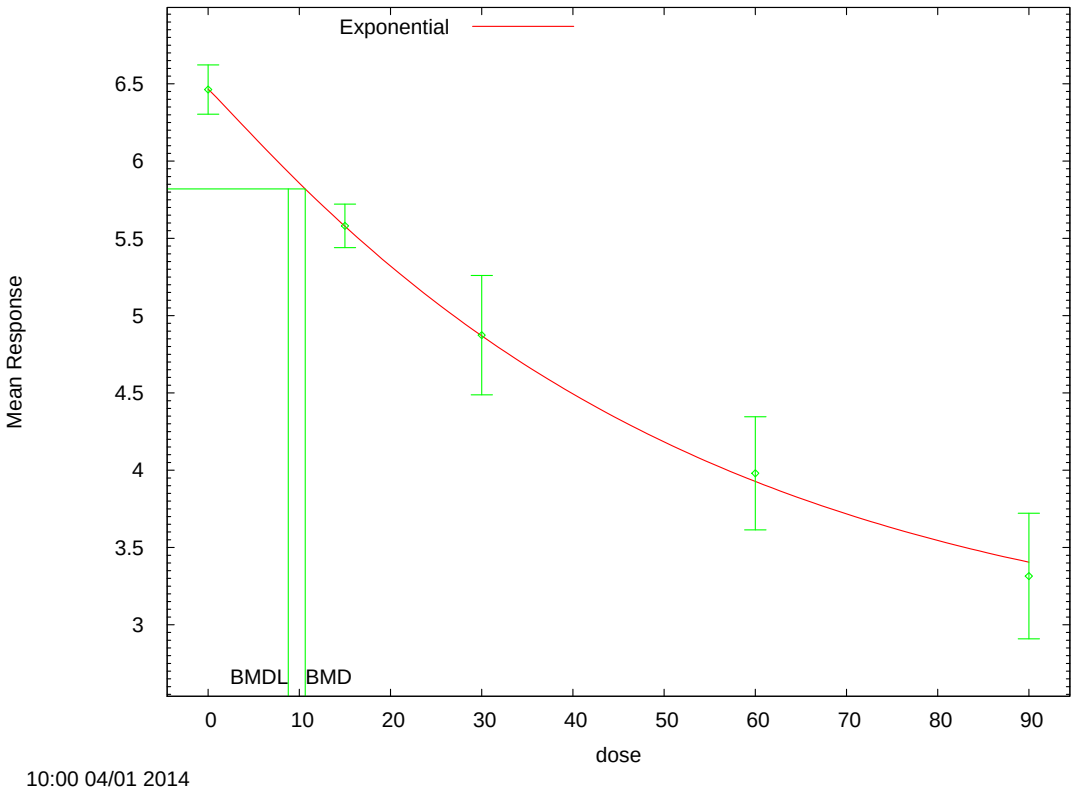
10:00 04/01 2014

Exponential Model 4, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



10:00 04/01 2014

Exponential Model 5, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



10:00 04/01 2014

MRID 49037404 - Acute CCA Study – Female Pup Brain ChE PND12 – Non-Constant Variance

```
 ================================================================
        Exponential Model. (Version: 1.9;  Date: 01/29/2013)
        Input Data File: F:/Pirimiphos-methyl/BMD runs/exp_Acute CCA Female Pup PND12
Brain_Setting.(d)
        Gnuplot Plotting File:
                                                Tue Apr 01 11:11:32 2014
 ================================================================

 BMDS Model Run
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   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log(mean(i)) * rho)

   Total number of dose groups = 5
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha            2.7651            2.7651               2.7651            2.7651
         rho           -2.73049          -2.73049             -2.73049          -2.73049
           a            3.7355            2.64608              6.89955           6.89955
           b        0.00705496      -0.000125213           0.0123708         0.0123708
           c                --                --                0.252408
0.252408
           d                --                 2                  --                 1


                               Parameter Estimates by Model

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha        2.64461           2.64461           2.72485           2.72485
```

rho	-2.59545	-2.59545	-2.64366	-2.64366
a	6.51253	6.51253	6.52645	6.52645
b	0.00726732	0.00726732	0.00880322	0.00880323
c	--	--	0.134588	0.134589
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	6.571	0.387
15	10	5.666	0.239
30	10	5.387	0.515
60	10	4.121	0.442
90	10	3.483	0.904

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	6.513	0.3298	0.5606
	15	5.84	0.3799	-1.448
	30	5.237	0.4376	1.085
	60	4.211	0.5808	-0.4898
	90	3.386	0.7707	0.3977
3	0	6.513	0.3298	0.5606
	15	5.84	0.3799	-1.448
	30	5.237	0.4376	1.085
	60	4.211	0.5808	-0.4898
	90	3.386	0.7707	0.3977
4	0	6.526	0.3272	0.4306
	15	5.828	0.38	-1.346
	30	5.216	0.4401	1.232
	60	4.209	0.5843	-0.4755
	90	3.436	0.7641	0.1951
5	0	6.526	0.3272	0.4306
	15	5.828	0.38	-1.346
	30	5.216	0.4401	1.232
	60	4.209	0.5843	-0.4755
	90	3.436	0.7641	0.1951

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC

A1	7.989727	6	-3.979453
A2	17.24983	10	-14.49967
A3	13.57413	7	-13.14827
R	-35.00671	2	74.01341
2	12.0734	4	-16.1468
3	12.0734	4	-16.1468
4	12.11751	5	-14.23501
5	12.11751	5	-14.23501

Additive constant for all log-likelihoods = -45.95. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	104.5	8	< 0.0001
Test 2	18.52	4	0.0009762
Test 3	7.351	3	0.0615
Test 4	3.001	3	0.3914
Test 5a	3.001	3	0.3914
Test 5b	0	0	N/A
Test 6a	2.913	2	0.233
Test 6b	0.08821	1	0.7665
Test 7a	2.913	2	0.233
Test 7b	0.08821	1	0.7665
Test 7c	8.74e-013	0	N/A

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 4 is greater than .1. Model 2 seems to adequately describe the data.

The p-value for Test 5a is greater than .1. Model 3 seems to adequately describe the data.

Degrees of freedom for Test 5b are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

The p-value for Test 6b is greater than .05. Model 4 does not seem to fit the data better than Model 2.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

The p-value for Test 7b is greater than .05. Model 5 does not seem to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0. The Chi-Square test for fit is not valid.

Benchmark Dose Computations:

Specified Effect = 0.100000

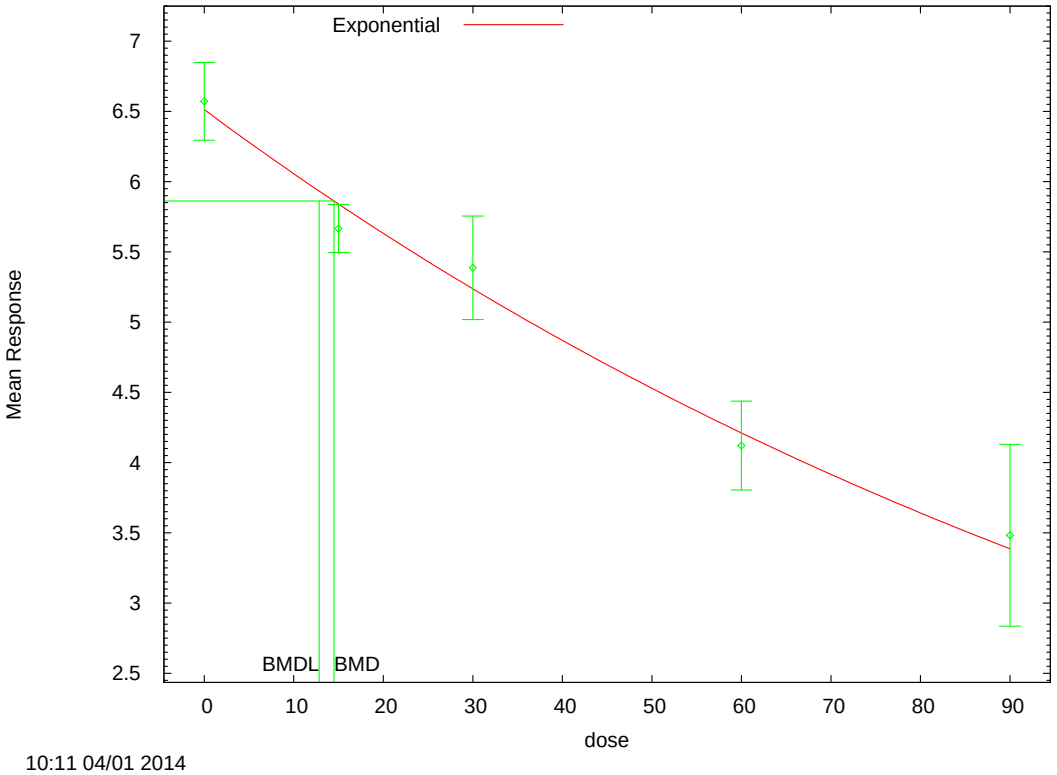
Risk Type = Relative deviation

Confidence Level = 0.950000

BMD and BMDL by Model

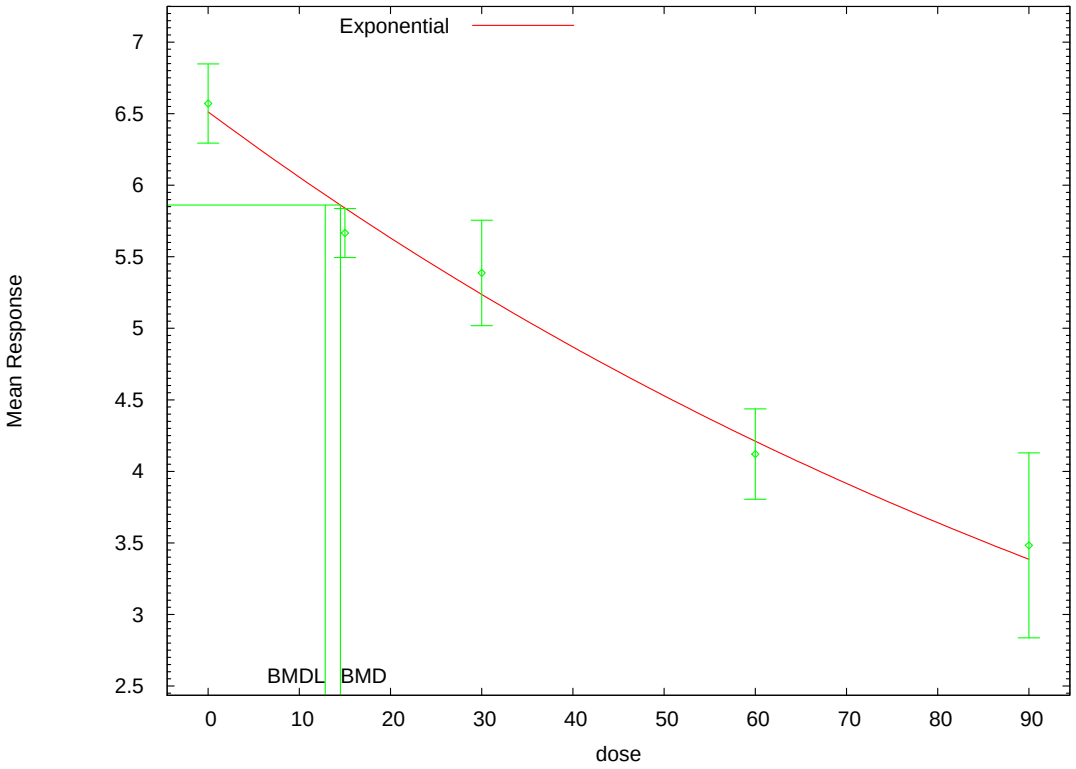
Model	BMD	BMDL
2	14.4978	12.8389
3	14.4978	12.8389
4	13.9485	10.9491
5	13.9485	10.9491

Exponential Model 2, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



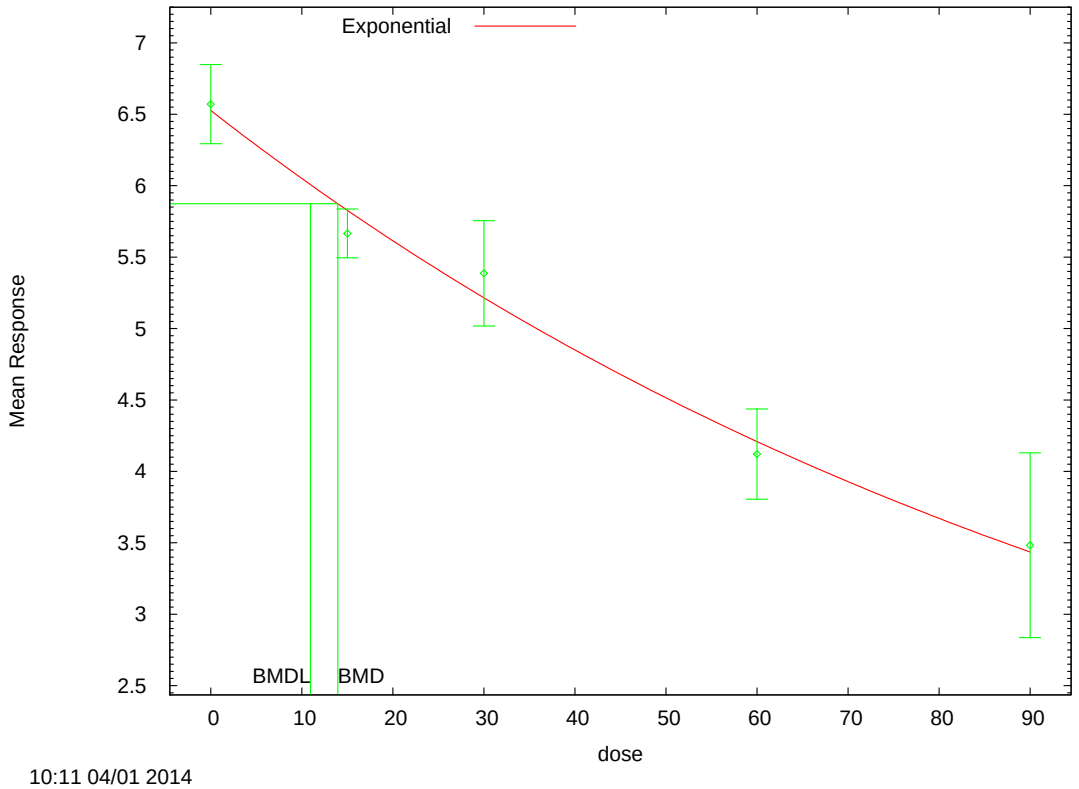
10:11 04/01 2014

Exponential Model 3, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



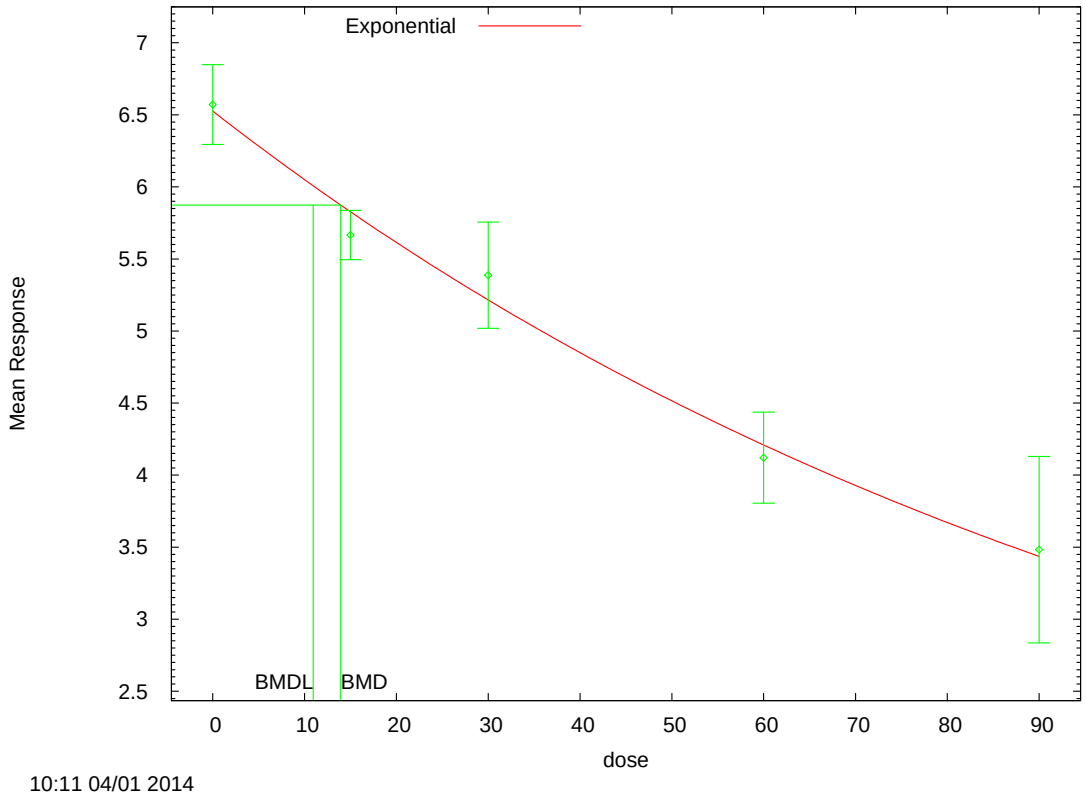
10:11 04/01 2014

Exponential Model 4, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



10:11 04/01 2014

Exponential Model 5, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



10:11 04/01 2014

MRID 43594101 - Acute Neurotoxicity Male RBC Day 1
CONSTANT VARIANCE - NO

```
 ================================================================
        Exponential Model. (Version: 1.7;  Date: 12/10/2009)
        Input Data File: C:/Users/EHolman/Desktop/HED Desktop/BMDS220/Data/exp_Acute
Neuro Male RBC Day 1_Setting.(d)
        Gnuplot Plotting File:
                                              Sat Apr 05 14:53:23 2014
 ================================================================

 BMDS Model Run
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   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log(mean(i)) * rho)

   Total number of dose groups = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 250
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha           5.79373           5.79373             5.79373           5.79373
         rho          0.580402          0.580402            0.580402          0.580402
           a           1082.75           1082.75              2496.9            2496.9
           b       0.000677917       0.000677917          0.00270191        0.00270191
           c                --                --                0.267379
0.267379
           d                --                 1                  --                 1


                               Parameter Estimates by Model

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
```

lnalpha	-5.75775	-5.75775	-3.66224	-3.66224
rho	2.33169	2.33169	1.9714	1.9714
a	1927.89	1927.89	2138.52	2138.52
b	0.000682958	0.000682958	0.00478888	0.00478888
c	--	--	0.329596	0.329596
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	5	2378	150
15	5	1758	294.6
150	5	1450	86.8
1500	5	701	129.8

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	1928	379.9	2.65
	15	1908	375.3	-0.895
	150	1740	337.1	-1.925
	1500	692.1	115.1	0.1728
3	0	1928	379.9	2.65
	15	1908	375.3	-0.895
	150	1740	337.1	-1.925
	1500	692.1	115.1	0.1728
4	0	2139	307.1	1.744
	15	2039	293	-2.146
	150	1404	202.8	0.5088
	1500	705.9	103	-0.1072
5	0	2139	307.1	1.744
	15	2039	293	-2.146
	150	1404	202.8	0.5088
	1500	705.9	103	-0.1072

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-111.937	5	233.874
A2	-107.8978	8	231.7957
A3	-111.3484	6	234.6968

R	-138.7691	2	281.5381
2	-122.1672	4	252.3345
3	-122.1672	4	252.3345
4	-116.7704	5	243.5407
5	-116.7704	5	243.5407

Additive constant for all log-likelihoods = -18.38. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	61.74	6	< 0.0001
Test 2	8.078	3	0.04442
Test 3	6.901	2	0.03173
Test 4	21.64	2	< 0.0001
Test 5a	21.64	2	< 0.0001
Test 5b	-1.99e-013	0	N/A
Test 6a	10.84	1	0.0009912
Test 6b	10.79	1	0.001018
Test 7a	10.84	1	0.0009912
Test 7b	10.79	1	0.001018
Test 7c	0	0	N/A

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 4 is less than .1. Model 2 may not adequately describe the data; you may want to consider another model.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Degrees of freedom for Test 5b are less than or equal to 0.
The Chi-Square test for fit is not valid.

The p-value for Test 6a is less than .1. Model 4 may not adequately describe the data; you may want to consider another model.

The p-value for Test 6b is less than .05. Model 4 appears to fit the data better than Model 2.

The p-value for Test 7a is less than .1. Model 5 may not adequately describe the data; you may want to consider another model.

The p-value for Test 7b is less than .05. Model 5 appears to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0.
The Chi-Square test for fit is not valid.

Benchmark Dose Computations:

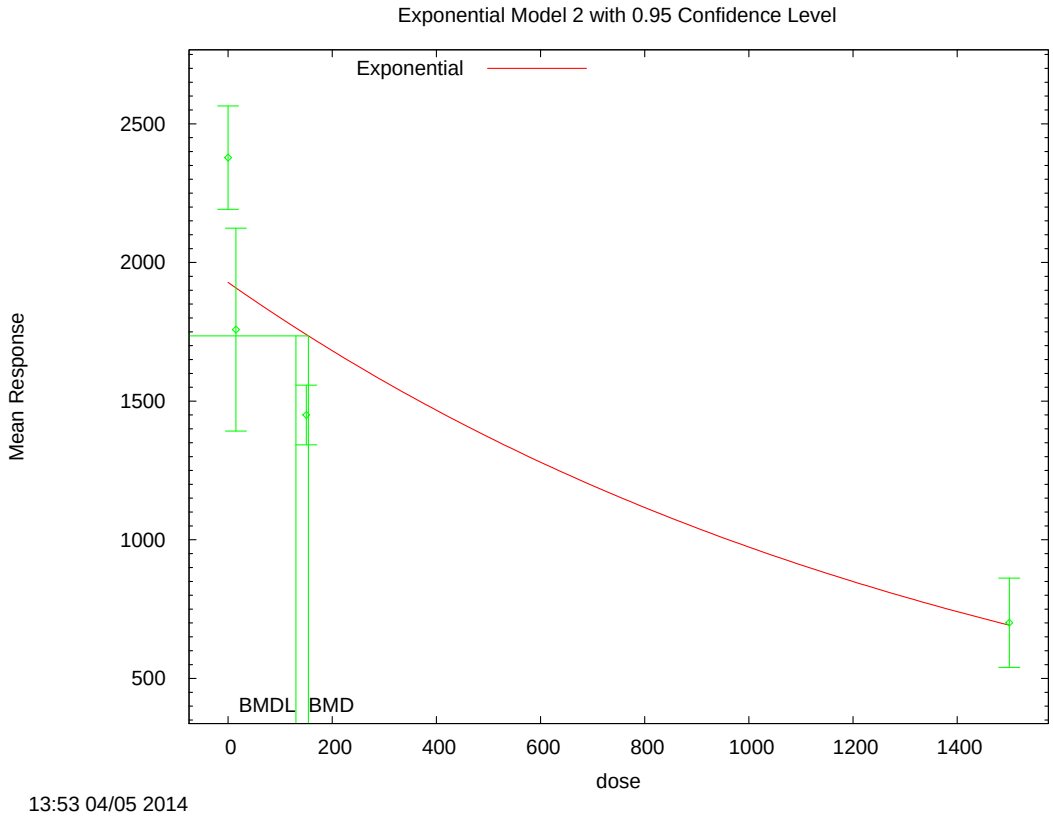
Specified Effect = 0.100000

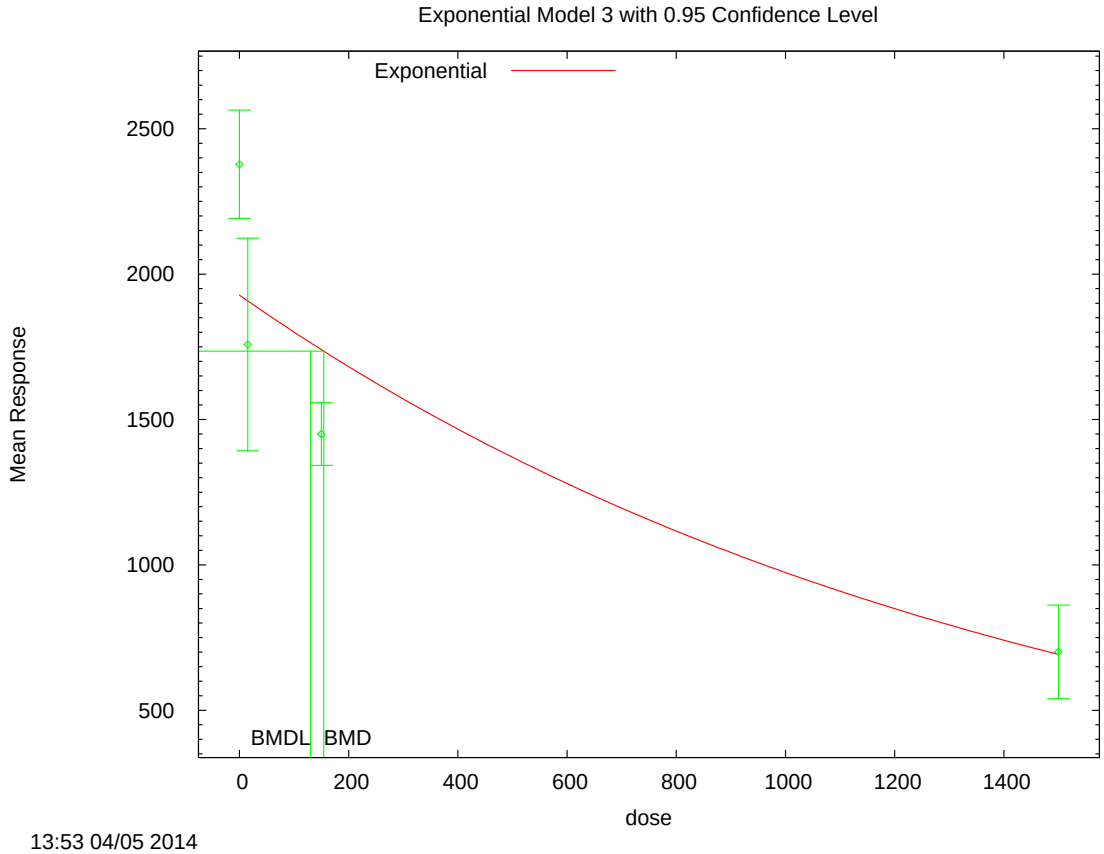
Risk Type = Relative deviation

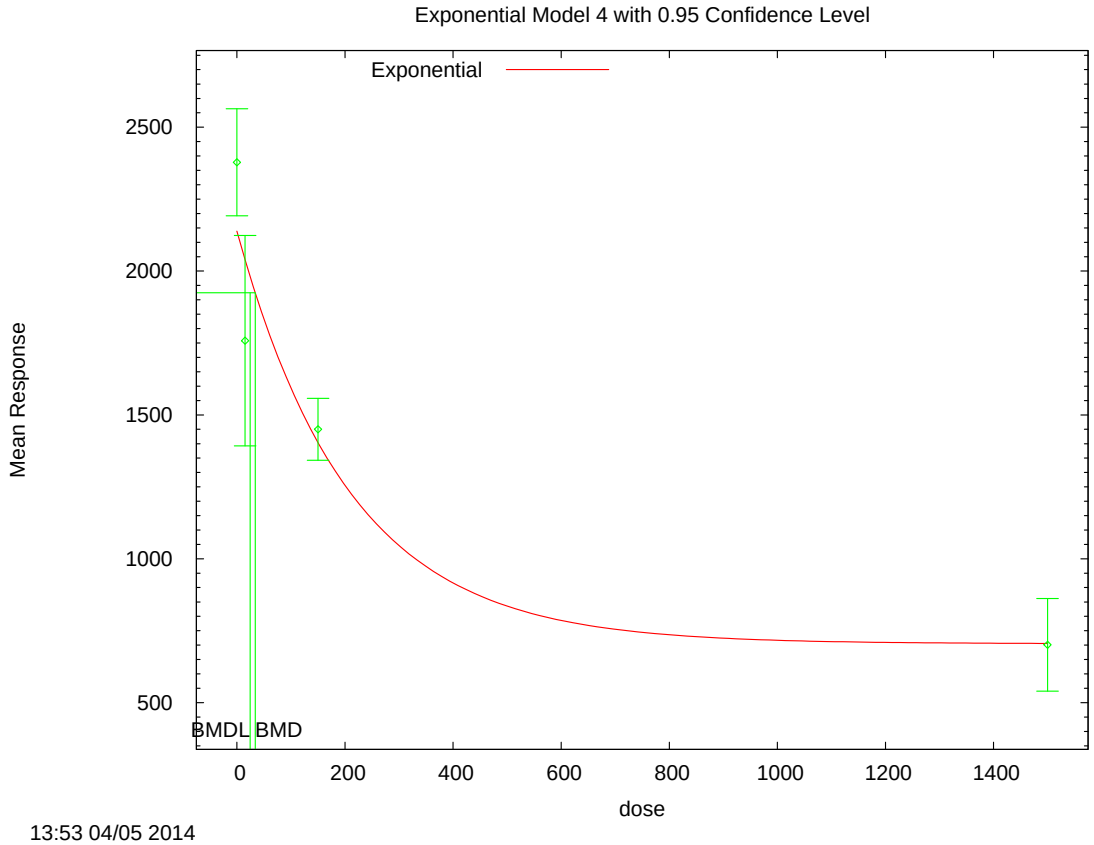
Confidence Level = 0.950000

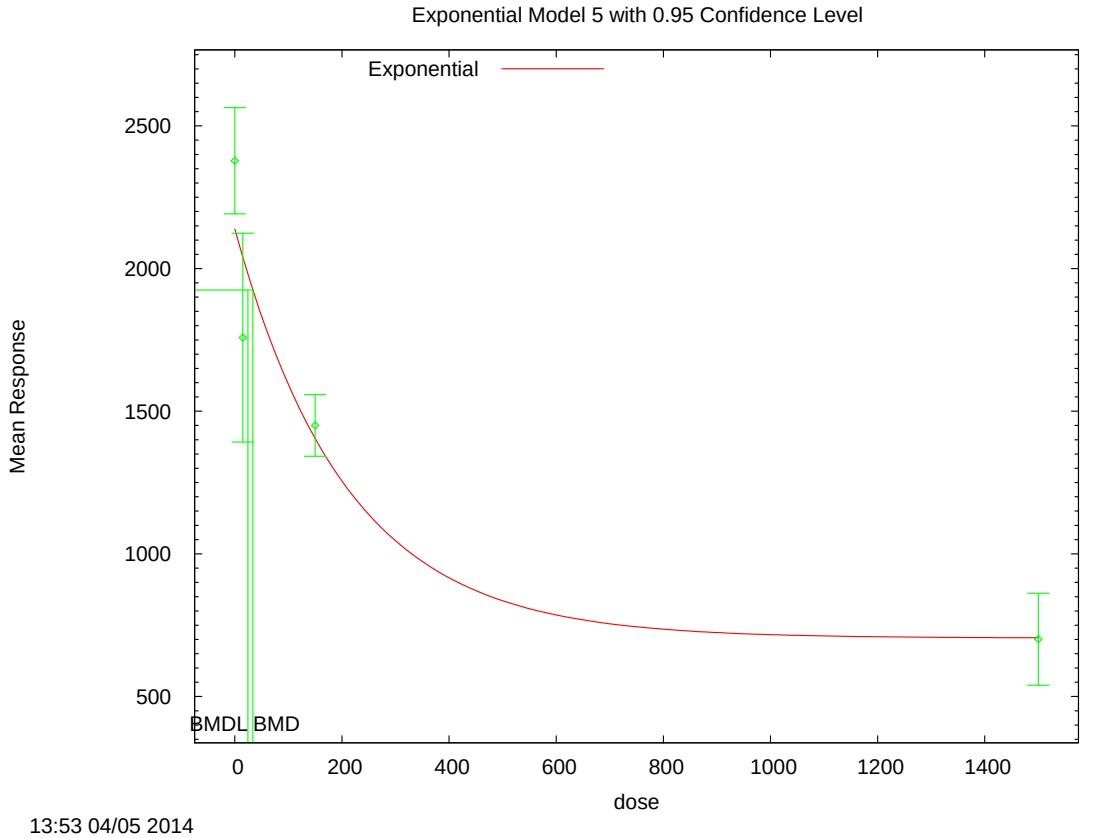
BMD and BMDL by Model

Model	BMD	BMDL
2	154.271	130.172
3	154.271	130.172
4	33.7314	24.3629
5	33.7314	24.3629


Exponential Model 2 with 0.95 Confidence Level
Exponential
Mean Response
2500
2000
1500
1000
500
BMDL
BMD
0
200
400
600
800
1000
1200
1400
dose
13:53 04/05 2014


Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
2500
2000
1500
1000
500
BMDL
BMD
0
200
400
600
800
1000
1200
1400
dose
13:53 04/05 2014


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
2500
2000
1500
1000
500
BMDL BMD
0
200
400
600
800
1000
1200
1400
dose
13:53 04/05 2014


Exponential Model 5 with 0.95 Confidence Level
Exponential
Mean Response
2500
2000
1500
1000
500
BMDL BMD
0
200
400
600
800
1000
1200
1400
dose
13:53 04/05 2014

MRID 43594101 - Acute Neurotoxicity Female RBC Day 1
CONSTANT VARIANCE - NO

```
 ================================================================
        Exponential Model. (Version: 1.7;  Date: 12/10/2009)
        Input Data File: C:/Users/EHolman/Desktop/HED Desktop/BMDS220/Data/exp_Acute
Neuro Female RBC Day 1_Setting.(d)
        Gnuplot Plotting File:
                                              Sat Apr 05 15:37:42 2014
 ================================================================

 BMDS Model Run
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   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log(mean(i)) * rho)

   Total number of dose groups = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 250
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha          -5.34012          -5.34012           -5.34012          -5.34012
         rho           2.10267           2.10267            2.10267           2.10267
           a           1194.41           1194.41            2233.35           2233.35
           b       0.000620403       0.000620403         0.00244897        0.00244897
           c                --                --               0.339443
0.339443
           d                --                 1                  --                 1


                               Parameter Estimates by Model

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
```

lnalpha	-9.06547	-9.06546	-7.24038	-7.24038
rho	2.62792	2.62792	2.34692	2.34692
a	2002.33	2002.33	2099.07	2099.07
b	0.000618136	0.000618136	0.00259262	0.00259262
c	--	--	0.366361	0.366361
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	5	2127	161.1
15	5	2015	298.1
150	5	1676	160.2
1500	5	796	77.2

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	2002	234.2	1.19
	15	1984	231.3	0.3011
	150	1825	207.3	-1.607
	1500	792.2	69.25	0.1214
3	0	2002	234.2	1.19
	15	1984	231.3	0.3011
	150	1825	207.3	-1.607
	1500	792.2	69.25	0.1214
4	0	2099	211.9	0.2947
	15	2048	205.9	-0.3622
	150	1671	162.1	0.07535
	1500	796.2	67.93	-0.007972
5	0	2099	211.9	0.2947
	15	2048	205.9	-0.3622
	150	1671	162.1	0.07535
	1500	796.2	67.93	-0.007972

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-112.8494	5	235.6988
A2	-108.7799	8	233.5599
A3	-109.9195	6	231.839

R	-136.1806	2	276.3612
2	-112.3598	4	232.7197
3	-112.3598	4	232.7197
4	-109.9474	5	229.8947
5	-109.9474	5	229.8947

Additive constant for all log-likelihoods = -18.38. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	54.8	6	< 0.0001
Test 2	8.139	3	0.04323
Test 3	2.279	2	0.32
Test 4	4.881	2	0.08713
Test 5a	4.881	2	0.08713
Test 5b	-2.842e-012	0	N/A
Test 6a	0.05576	1	0.8133
Test 6b	4.825	1	0.02805
Test 7a	0.05576	1	0.8133
Test 7b	4.825	1	0.02805
Test 7c	2.842e-014	0	N/A

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is less than .1. Model 2 may not adequately describe the data; you may want to consider another model.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Degrees of freedom for Test 5b are less than or equal to 0.
The Chi-Square test for fit is not valid.

The p-value for Test 6a is greater than .1. Model 4 seems
to adequately describe the data.

The p-value for Test 6b is less than .05. Model 4 appears
to fit the data better than Model 2.

The p-value for Test 7a is greater than .1. Model 5 seems
to adequately describe the data.

The p-value for Test 7b is less than .05. Model 5 appears
to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0.
The Chi-Square test for fit is not valid.

Benchmark Dose Computations:

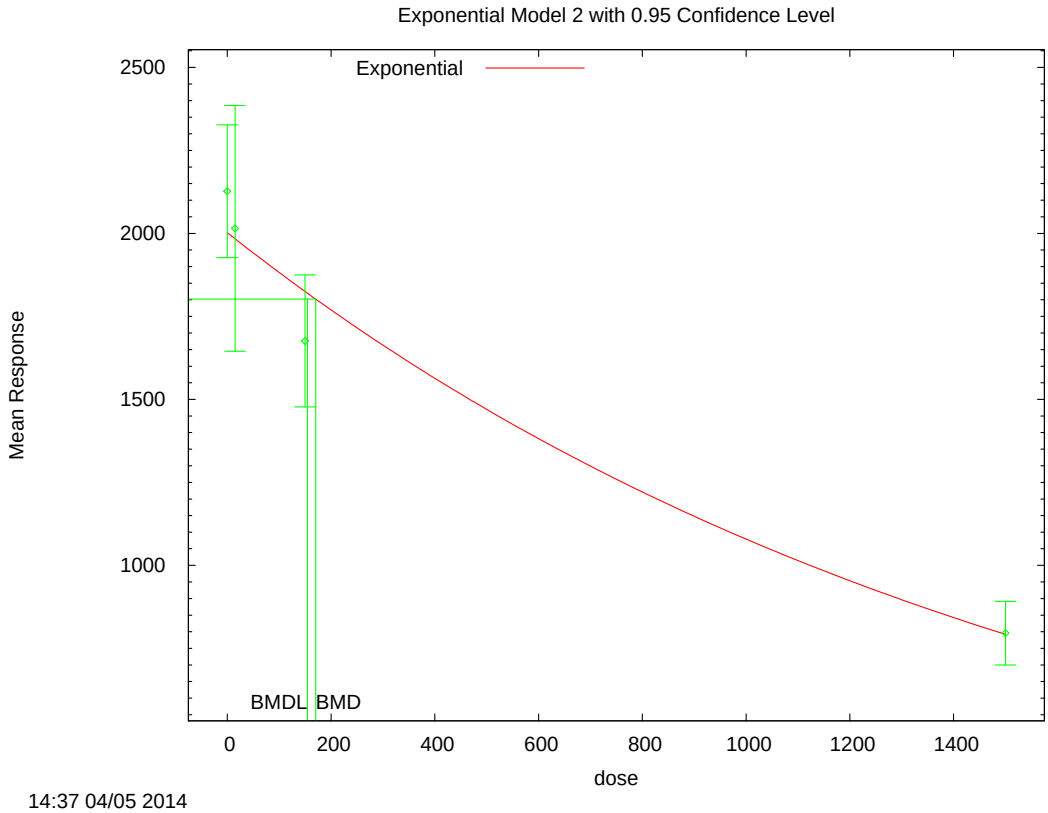
Specified Effect = 0.100000

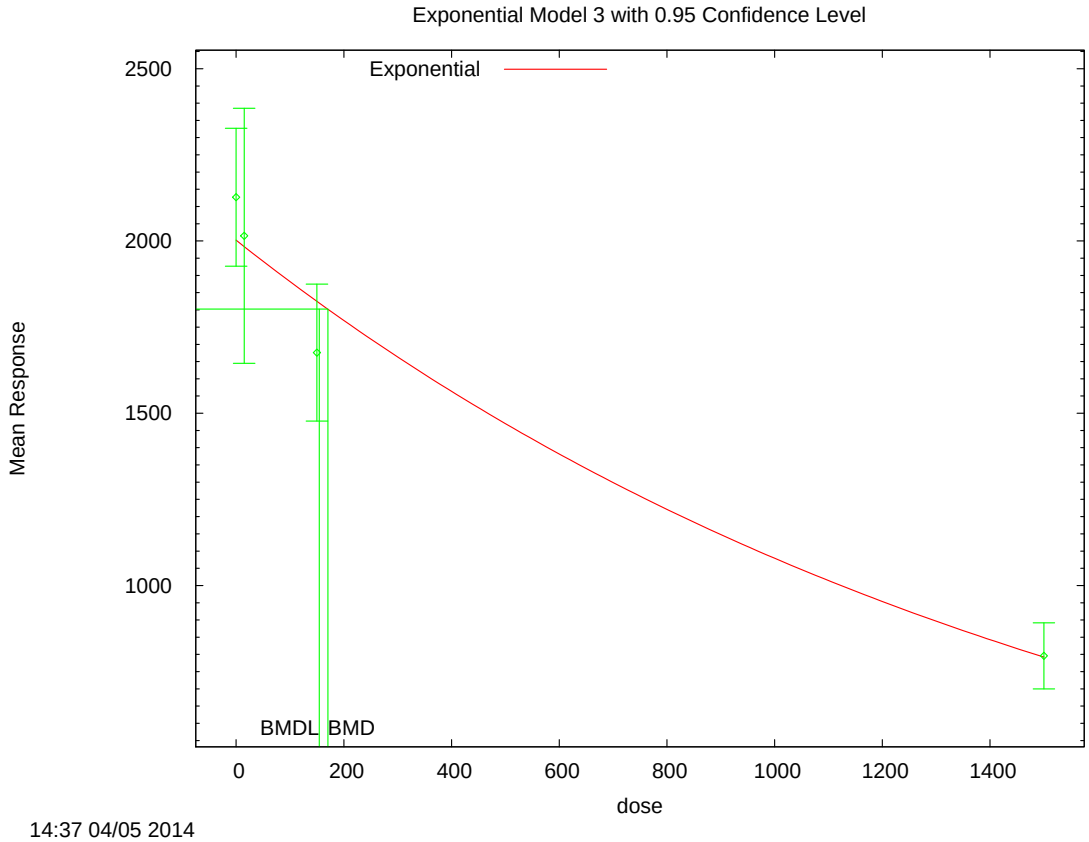
Risk Type = Relative deviation

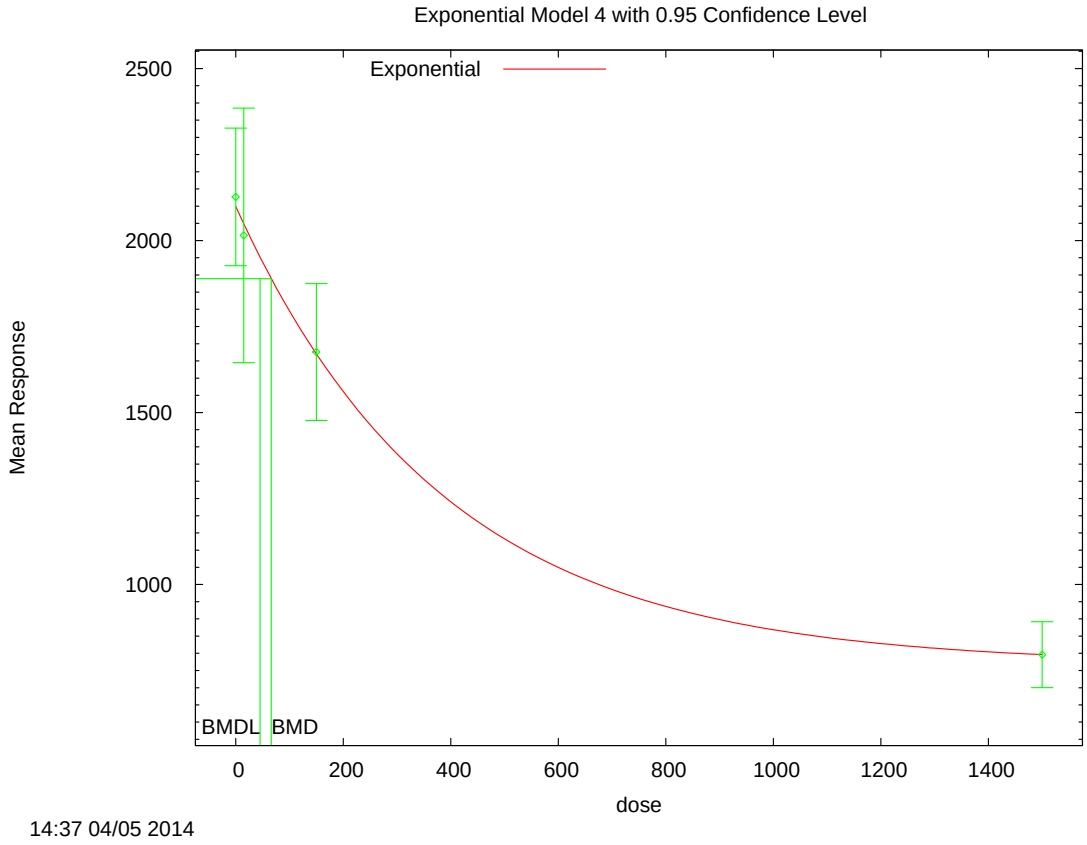
Confidence Level = 0.950000

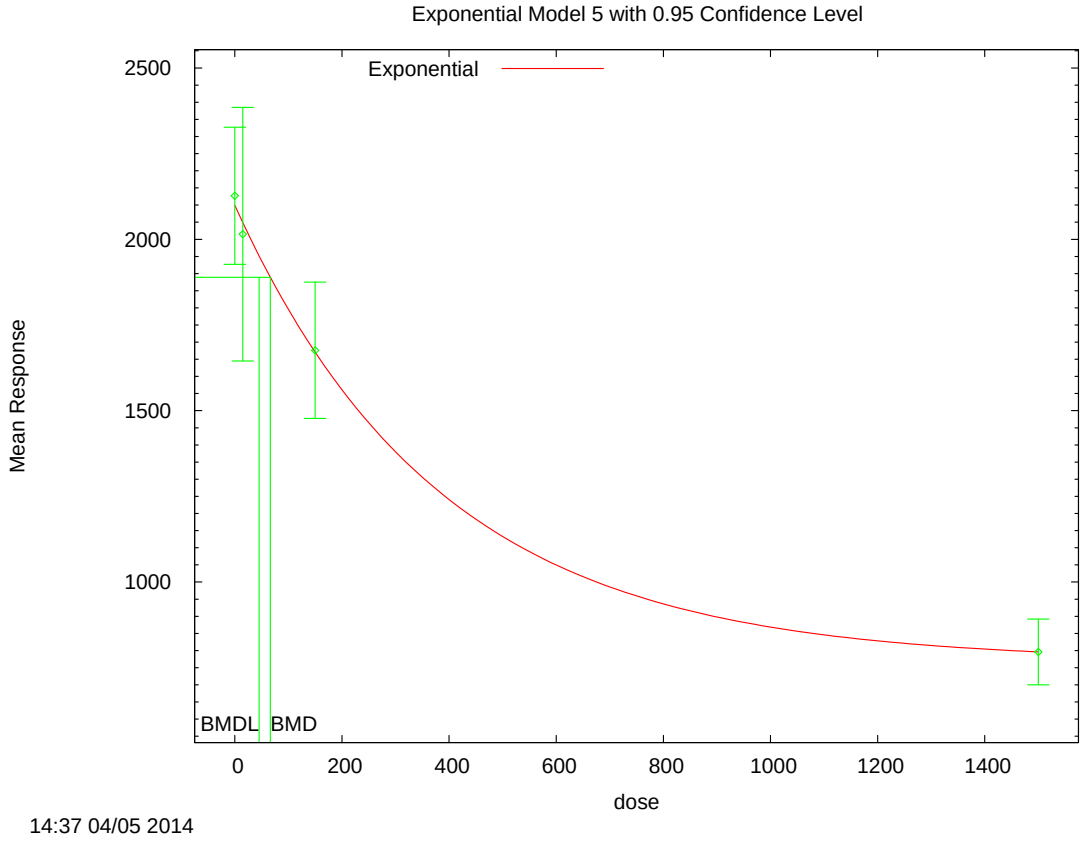
BMD and BMDL by Model

Model	BMD	BMDL
2	170.449	154.41
3	170.449	154.41
4	66.2495	45.2475
5	66.2495	45.2475


Exponential Model 2 with 0.95 Confidence Level
Exponential
2500
2000
1500
1000
Mean Response
BMDL BMD
0
200
400
600
800
1000
1200
1400
dose
14:37 04/05 2014


Exponential Model 3 with 0.95 Confidence Level
Exponential
2500
2000
1500
1000
Mean Response
BMDL BMD
0
200
400
600
800
1000
1200
1400
dose
14:37 04/05 2014


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
2500
2000
1500
1000
0
200
400
600
800
1000
1200
1400
14:37 04/05 2014


Exponential Model 5 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
2500
2000
1500
1000
0
200
400
600
800
1000
1200
1400
14:37 04/05 2014

MRID 43594101 - Acute Neurotoxicity Male RBC Day 15
CONSTANT VARIANCE - YES

```
 ======================================================================
        Exponential Model. (Version: 1.7;  Date: 12/10/2009)
        Input Data File: C:/Users/EHolman/Desktop/HED Desktop/BMDS220/Data/exp_Acute
Neuro Male RBC Day 15_Setting.(d)
        Gnuplot Plotting File:
                                              Sat Apr 05 14:58:14 2014
 ======================================================================

 BMDS Model Run
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   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 250
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha           9.84396           9.84396             9.84396           9.84396
         rho(S)              0                 0                   0                 0
           a           1950.74           1950.74              2289              2289
           b       8.0253e-005       8.0253e-005         0.00124882        0.00124882
           c                --                --                0.77472
0.77472
           d                --                 1                  --                 1

     (S) = Specified
```

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	10.194	10.194	9.84399	9.84399
rho	0	0	0	0
a	2089.38	2089.38	2179.26	2179.26
b	8.25424e-005	8.25424e-005	0.011765	0.011765
c	--	--	0.854526	0.854526
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	5	2180	80.7
15	5	2127	189.7
150	5	1917	165.3
1500	5	1862	156.2

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	2089	163.5	1.239
	15	2087	163.5	0.5498
	150	2064	163.5	-2.005
	1500	1846	163.5	0.218
3	0	2089	163.5	1.239
	15	2087	163.5	0.5498
	150	2064	163.5	-2.005
	1500	1846	163.5	0.218
4	0	2179	137.3	0.01199
	15	2128	137.3	-0.01589
	150	1917	137.3	0.007779
	1500	1862	137.3	-0.003876
5	0	2179	137.3	0.01199
	15	2128	137.3	-0.01589
	150	1917	137.3	0.007779
	1500	1862	137.3	-0.003876

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC

A1	-108.4396	5	226.8792
A2	-106.744	8	229.4879
A3	-108.4396	5	226.8792
R	-115.186	2	234.3721
2	-111.9402	3	229.8805
3	-111.9402	3	229.8805
4	-108.4399	4	224.8797
5	-108.4399	4	224.8797

Additive constant for all log-likelihoods = -18.38. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	16.88	6	0.009719
Test 2	3.391	3	0.3351
Test 3	3.391	3	0.3351
Test 4	7.001	2	0.03018
Test 5a	7.001	2	0.03018
Test 5b	-8.527e-014	0	N/A
Test 6a	0.0004718	1	0.9827
Test 6b	7.001	1	0.008147
Test 7a	0.0004718	1	0.9827
Test 7b	7.001	1	0.008147
Test 7c	1.137e-013	0	N/A

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is greater than .1. A homogeneous variance model appears to be appropriate here.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is less than .1. Model 2 may not adequately describe the data; you may want to consider another model.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Degrees of freedom for Test 5b are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

The p-value for Test 6b is less than .05. Model 4 appears to fit the data better than Model 2.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

The p-value for Test 7b is less than .05. Model 5 appears to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0. The Chi-Square test for fit is not valid.

Benchmark Dose Computations:

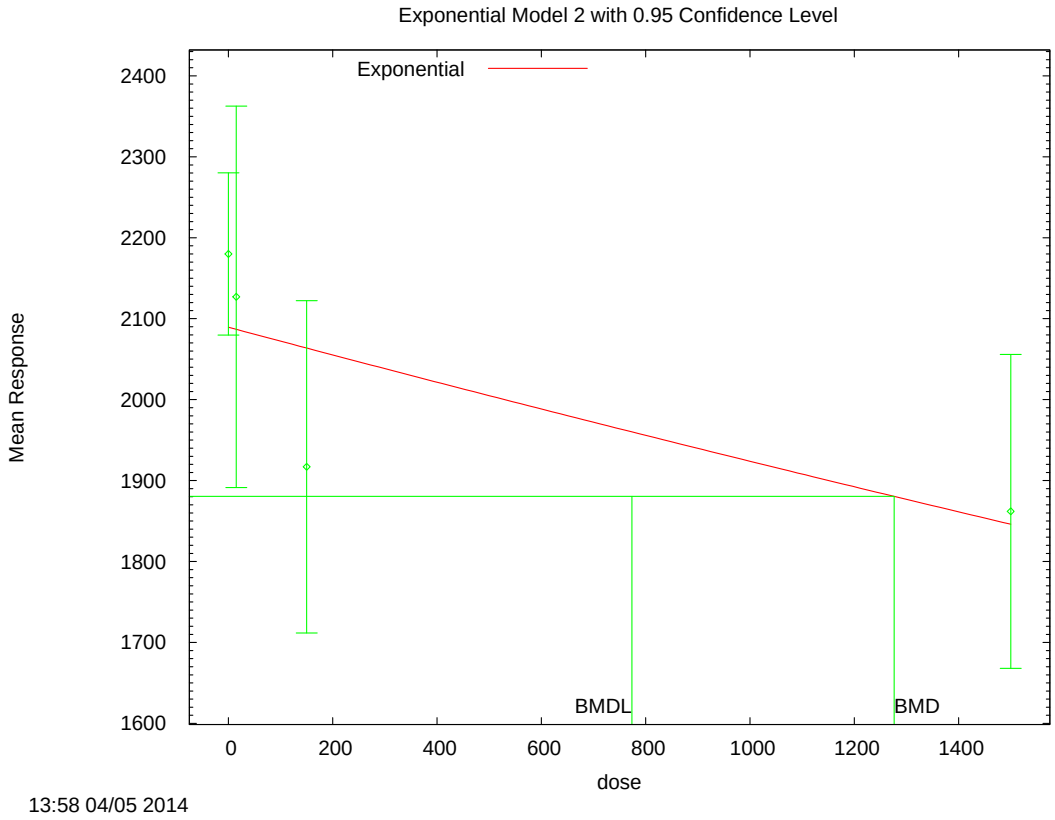
Specified Effect = 0.100000

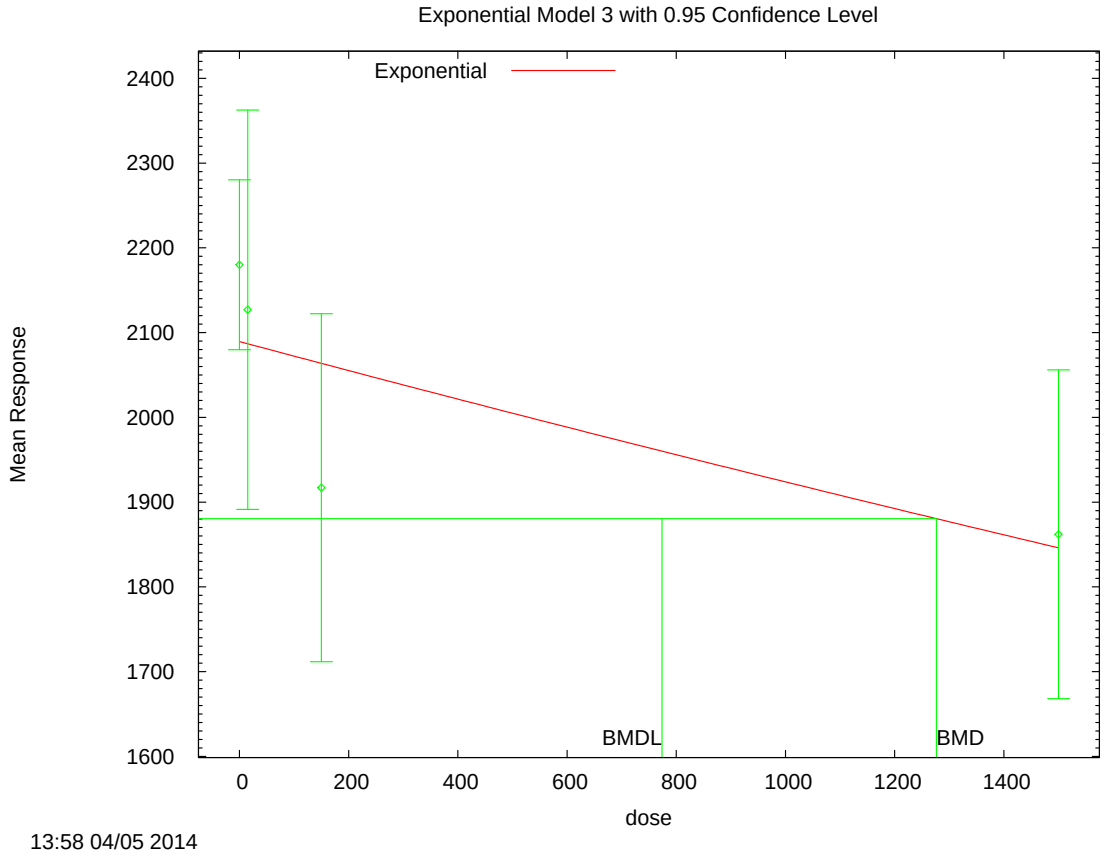
Risk Type = Relative deviation

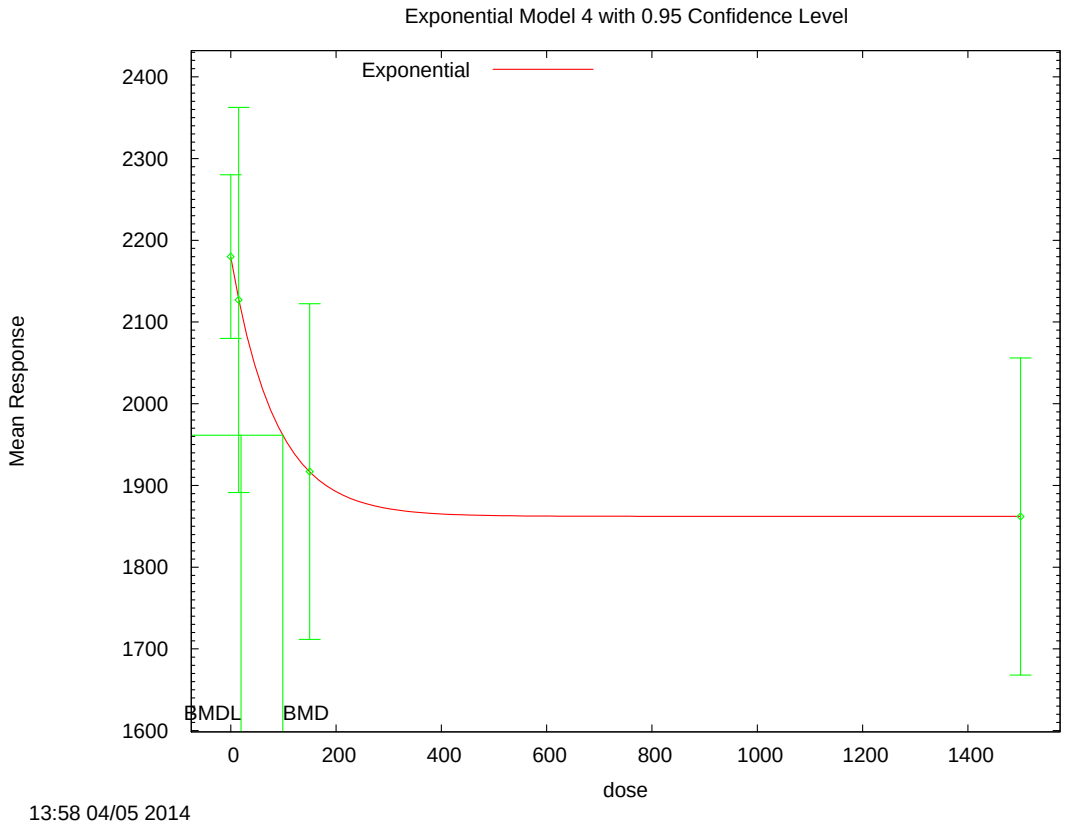
Confidence Level = 0.950000

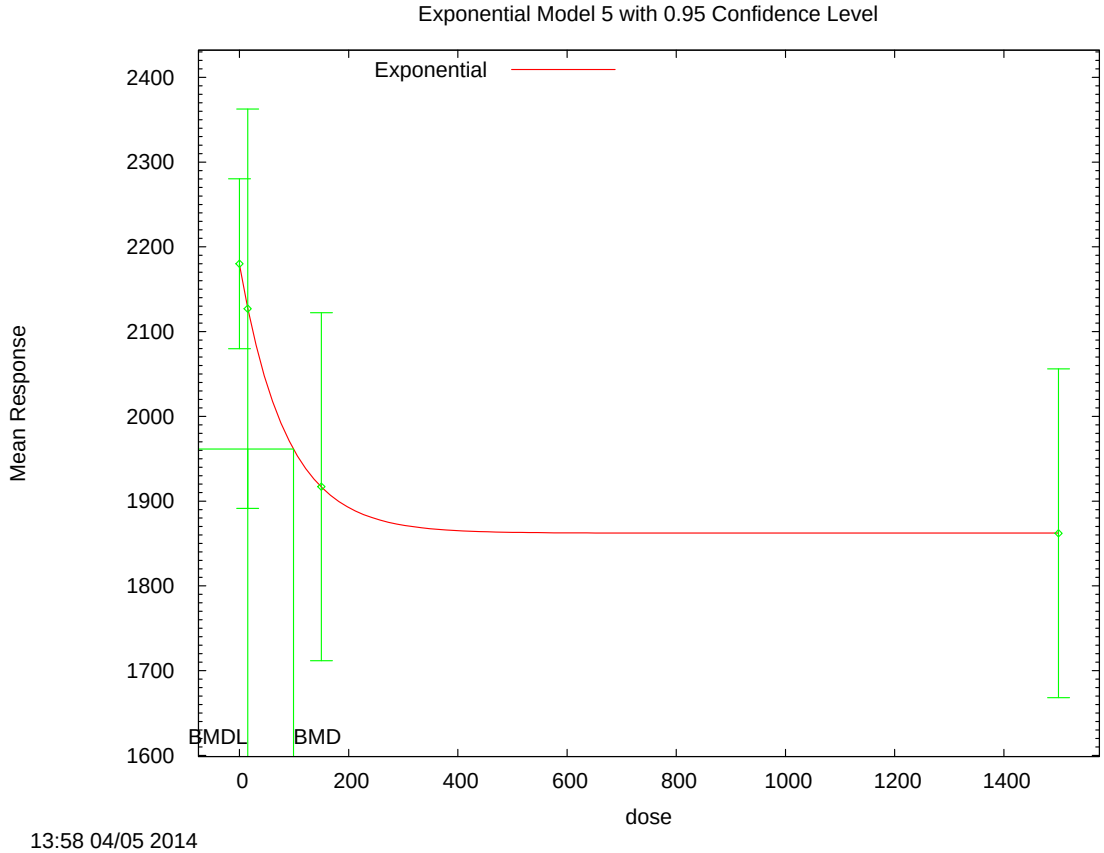
BMD and BMDL by Model

Model	BMD	BMDL
2	1276.44	773.708
3	1276.44	773.708
4	98.8407	19.5423
5	98.8407	15.2227


Exponential Model 2 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
2400
2300
2200
2100
2000
1900
1800
1700
1600
0
200
400
600
800
1000
1200
1400
13:58 04/05 2014


Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
2400
2300
2200
2100
2000
1900
1800
1700
1600
0
200
400
600
800
1000
1200
1400
13:58 04/05 2014


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
2400
2300
2200
2100
2000
1900
1800
1700
1600
0
200
400
600
800
1000
1200
1400
13:58 04/05 2014


Exponential Model 5 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
2400
2300
2200
2100
2000
1900
1800
1700
1600
0
200
400
600
800
1000
1200
1400
13:58 04/05 2014

MRID 43594101 - Acute Neurotoxicity Male Midbrain Day 1
CONSTANT VARIANCE - YES

```
 ================================================================
        Exponential Model. (Version: 1.7;  Date: 12/10/2009)
        Input Data File: C:/Users/EHolman/Desktop/HED Desktop/BMDS220/Data/exp_Acute
Neuro Male Midbrain Day 1_Setting.(d)
        Gnuplot Plotting File:
                                              Sat Apr 05 15:09:04 2014
 ================================================================

 BMDS Model Run
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   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 250
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha          -1.38377          -1.38377           -1.38377          -1.38377
         rho(S)              0                 0                  0                 0
           a           5.54986           5.54986            11.4345           11.4345
           b       0.000714556       0.000714556          0.00260347        0.00260347
           c                --                --               0.289017
0.289017
           d                --                 1                  --                 1

     (S) = Specified


                             Parameter Estimates by Model
```

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	-0.660026	-0.660026	-1.0853	-1.0853
rho	0	0	0	0
a	10.1465	10.1465	10.5054	10.5054
b	0.000752309	0.000752309	0.00235796	0.00235796
c	--	--	0.310551	0.310551
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	5	10.89	0.539
15	5	9.81	0.413
150	5	8.41	0.769
1500	5	3.47	0.448

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	10.15	0.7189	2.313
	15	10.03	0.7189	-0.6925
	150	9.064	0.7189	-2.033
	1500	3.283	0.7189	0.5826
3	0	10.15	0.7189	2.313
	15	10.03	0.7189	-0.6925
	150	9.064	0.7189	-2.033
	1500	3.283	0.7189	0.5826
4	0	10.51	0.5812	1.48
	15	10.25	0.5812	-1.707
	150	8.348	0.5812	0.2399
	1500	3.473	0.5812	-0.0125
5	0	10.51	0.5812	1.48
	15	10.25	0.5812	-1.707
	150	8.348	0.5812	0.2399
	1500	3.473	0.5812	-0.0125

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	3.837735	5	2.324529

A2	5.071304	8	5.857391
A3	3.837735	5	2.324529
R	-31.17328	2	66.34656
2	-3.399745	3	12.79949
3	-3.399745	3	12.79949
4	0.8529568	4	6.294086
5	0.8529568	4	6.294086

Additive constant for all log-likelihoods = -18.38. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	72.49	6	< 0.0001
Test 2	2.467	3	0.4813
Test 3	2.467	3	0.4813
Test 4	14.47	2	0.0007191
Test 5a	14.47	2	0.0007191
Test 5b	-1.048e-013	0	N/A
Test 6a	5.97	1	0.01455
Test 6b	8.505	1	0.003541
Test 7a	5.97	1	0.01455
Test 7b	8.505	1	0.003541
Test 7c	-4.219e-015	0	N/A

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is greater than .1. A homogeneous variance model appears to be appropriate here.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is less than .1. Model 2 may not adequately describe the data; you may want to consider another model.

The p-value for Test 5a is less than .1. Model 3 may not adequately

describe the data; you may want to consider another model.

Degrees of freedom for Test 5b are less than or equal to 0.
The Chi-Square test for fit is not valid.

The p-value for Test 6a is less than .1. Model 4 may not adequately describe the data; you may want to consider another model.

The p-value for Test 6b is less than .05. Model 4 appears to fit the data better than Model 2.

The p-value for Test 7a is less than .1. Model 5 may not adequately describe the data; you may want to consider another model.

The p-value for Test 7b is less than .05. Model 5 appears to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0.
The Chi-Square test for fit is not valid.

Benchmark Dose Computations:

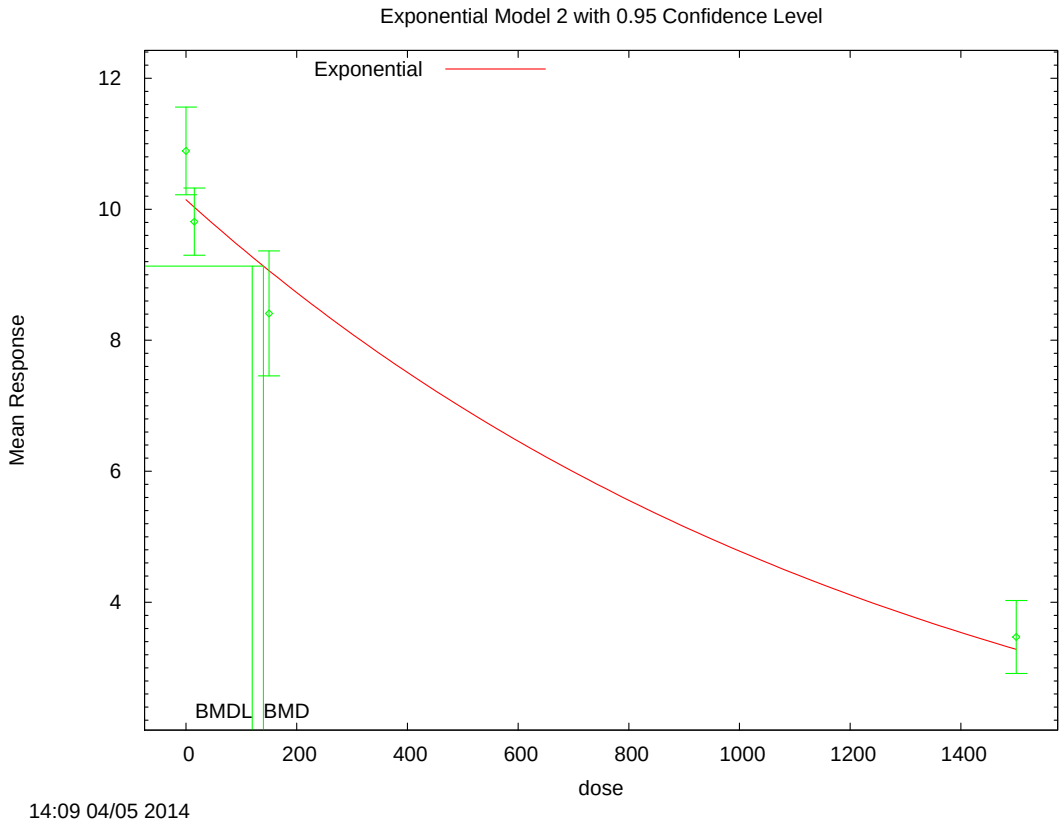
Specified Effect = 0.100000

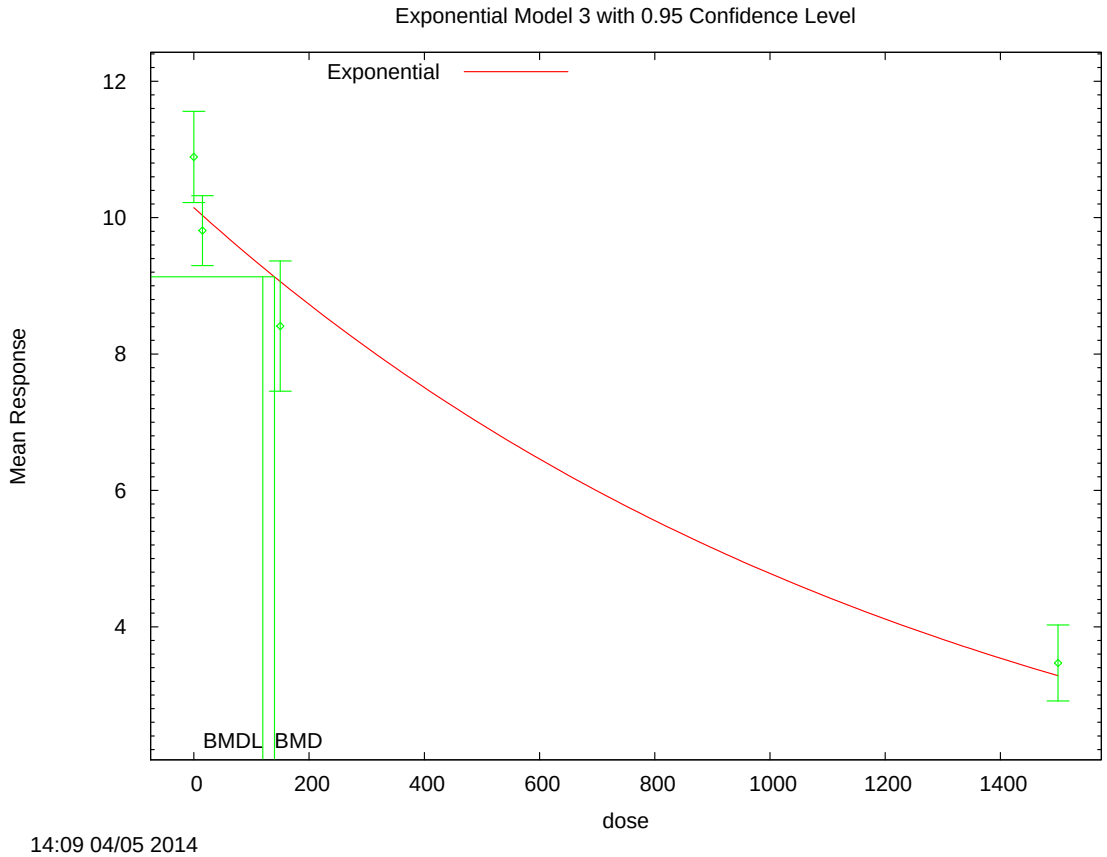
Risk Type = Relative deviation

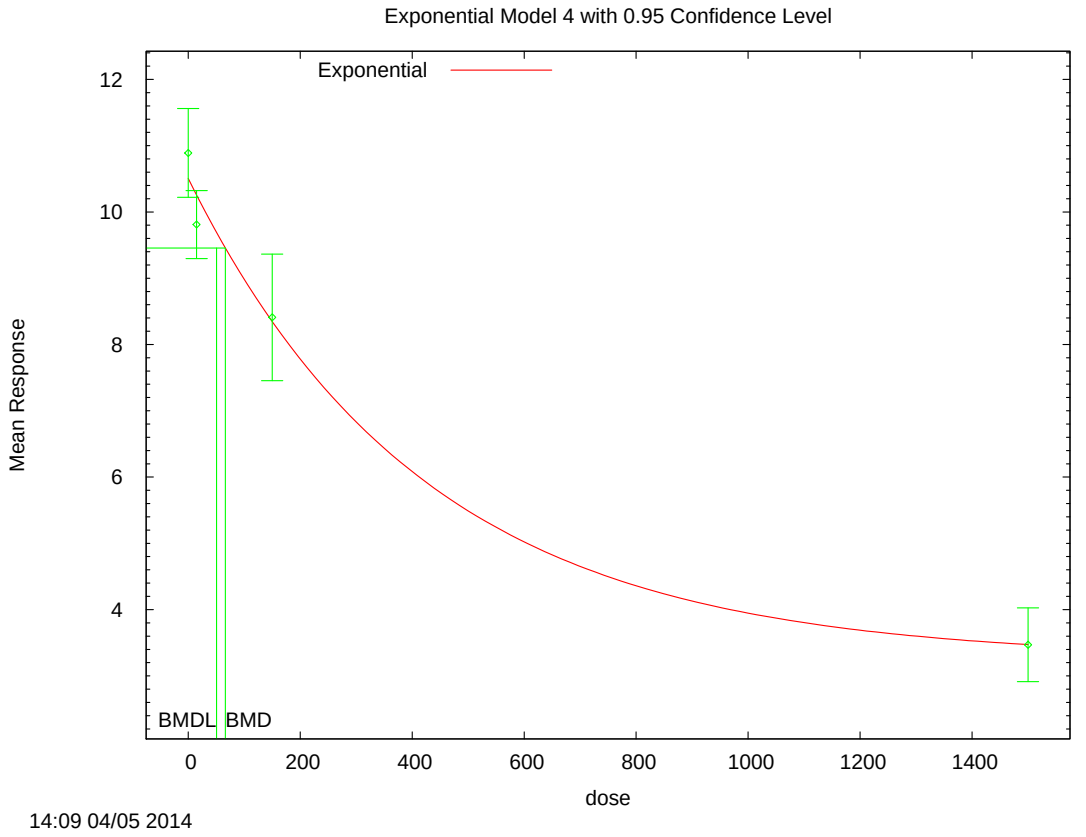
Confidence Level = 0.950000

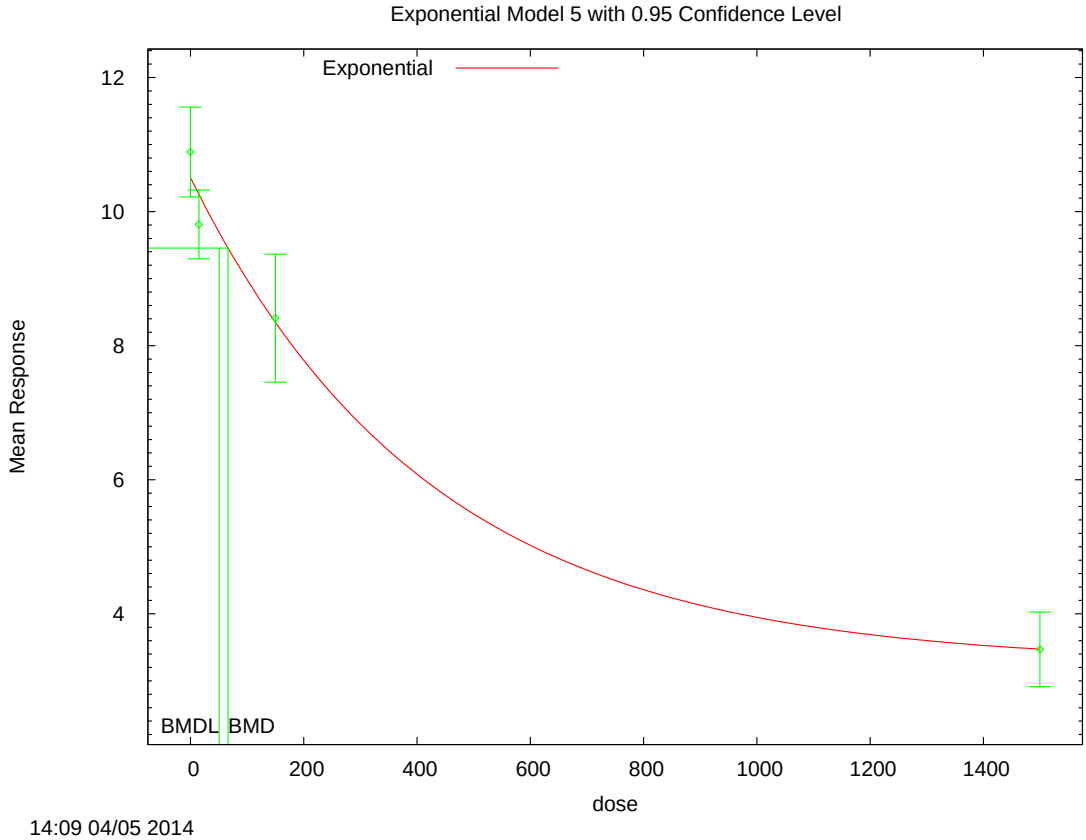
BMD and BMDL by Model

Model	BMD	BMDL
2	140.05	119.781
3	140.05	119.781
4	66.4576	50.5362
5	66.4576	50.5362


Exponential Model 2 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
12
10
8
6
4
0
200
400
600
800
1000
1200
1400
14:09 04/05 2014


Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
12
10
8
6
4
0
200
400
600
800
1000
1200
1400
14:09 04/05 2014


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
12
10
8
6
4
0
200
400
600
800
1000
1200
1400
14:09 04/05 2014


Exponential Model 5 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
12
10
8
6
4
0
200
400
600
800
1000
1200
1400
14:09 04/05 2014

MRID 43594101 - Acute Neurotoxicity Female Midbrain Day 1
CONSTANT VARIANCE - YES

```
 ================================================================
        Exponential Model. (Version: 1.7;  Date: 12/10/2009)
        Input Data File: C:/Users/EHolman/Desktop/HED Desktop/BMDS220/Data/exp_Acute
Neuro Female Midbrain Day 1_Setting.(d)
        Gnuplot Plotting File:
                                              Sat Apr 05 15:55:41 2014
 ================================================================

 BMDS Model Run
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   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 250
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha          -1.60933          -1.60933           -1.60933          -1.60933
         rho(S)              0                 0                  0                 0
           a           6.13445           6.13445            10.7415           10.7415
           b        0.00056268        0.00056268          0.00234024        0.00234024
           c                --                --               0.375934
0.375934
           d                --                 1                  --                 1

     (S) = Specified
```

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	-1.12251	-1.12251	-1.59062	-1.59062
rho	0	0	0	0
a	9.84923	9.84923	10.1498	10.1498
b	0.000581689	0.000581689	0.00217861	0.00217861
c	--	--	0.394749	0.394749
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	5	10.23	0.675
15	5	9.86	0.533
150	5	8.45	0.433
1500	5	4.24	0.27

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	9.849	0.5705	1.492
	15	9.764	0.5705	0.3776
	150	9.026	0.5705	-2.259
	1500	4.116	0.5705	0.4864
3	0	9.849	0.5705	1.492
	15	9.764	0.5705	0.3776
	150	9.026	0.5705	-2.259
	1500	4.116	0.5705	0.4864
4	0	10.15	0.4514	0.3972
	15	9.952	0.4514	-0.4572
	150	8.437	0.4514	0.06291
	1500	4.241	0.4514	-0.00295
5	0	10.15	0.4514	0.3972
	15	9.952	0.4514	-0.4572
	150	8.437	0.4514	0.06291
	1500	4.241	0.4514	-0.00295

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC

A1	6.093349	5	-2.186698
A2	8.074572	8	-0.1491442
A3	6.093349	5	-2.186698
R	-27.67321	2	59.34642
2	1.225146	3	3.549709
3	1.225146	3	3.549709
4	5.906236	4	-3.812472
5	5.906236	4	-3.812472

Additive constant for all log-likelihoods = -18.38. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	71.5	6	< 0.0001
Test 2	3.962	3	0.2655
Test 3	3.962	3	0.2655
Test 4	9.736	2	0.007687
Test 5a	9.736	2	0.007687
Test 5b	-1.048e-013	0	N/A
Test 6a	0.3742	1	0.5407
Test 6b	9.362	1	0.002215
Test 7a	0.3742	1	0.5407
Test 7b	9.362	1	0.002215
Test 7c	7.105e-015	0	N/A

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is greater than .1. A homogeneous variance model appears to be appropriate here.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is less than .1. Model 2 may not adequately describe the data; you may want to consider another model.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Degrees of freedom for Test 5b are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

The p-value for Test 6b is less than .05. Model 4 appears to fit the data better than Model 2.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

The p-value for Test 7b is less than .05. Model 5 appears to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0. The Chi-Square test for fit is not valid.

Benchmark Dose Computations:

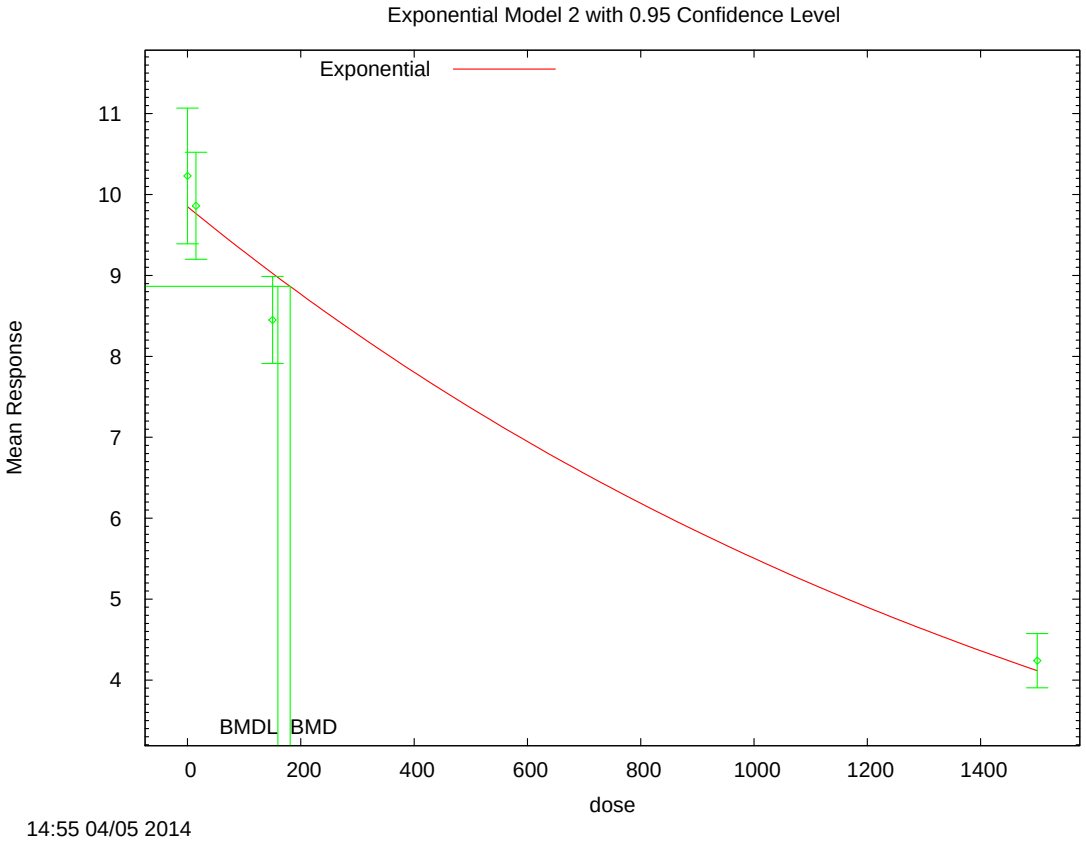
Specified Effect = 0.100000

Risk Type = Relative deviation

Confidence Level = 0.950000

BMD and BMDL by Model

Model	BMD	BMDL
2	181.128	159.565
3	181.128	159.565
4	82.8915	63.518
5	82.8915	63.518


Exponential Model 2 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
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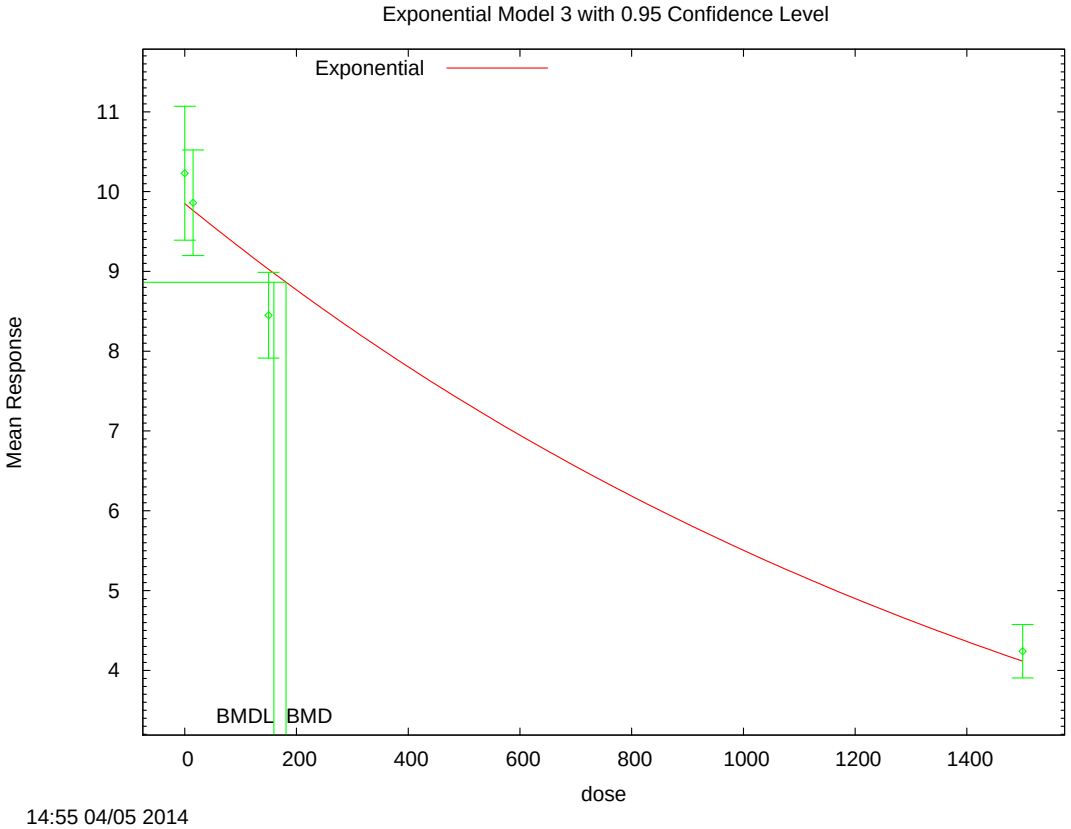
Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
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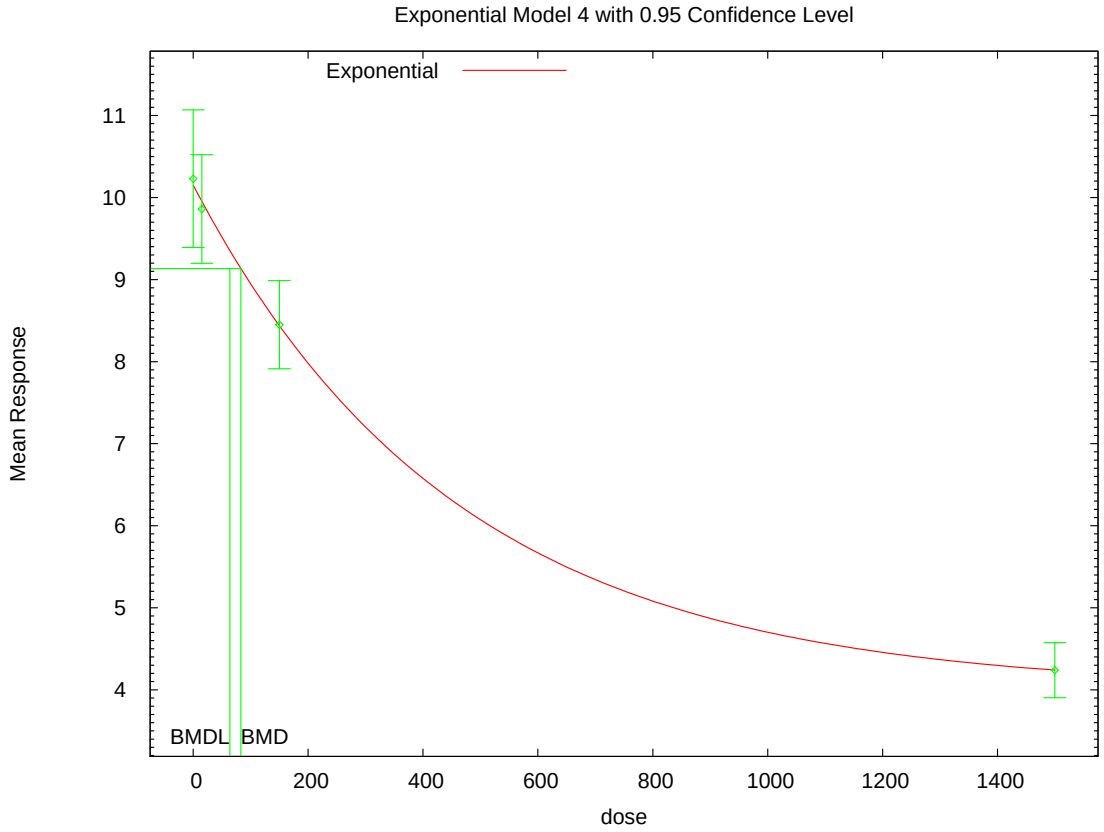

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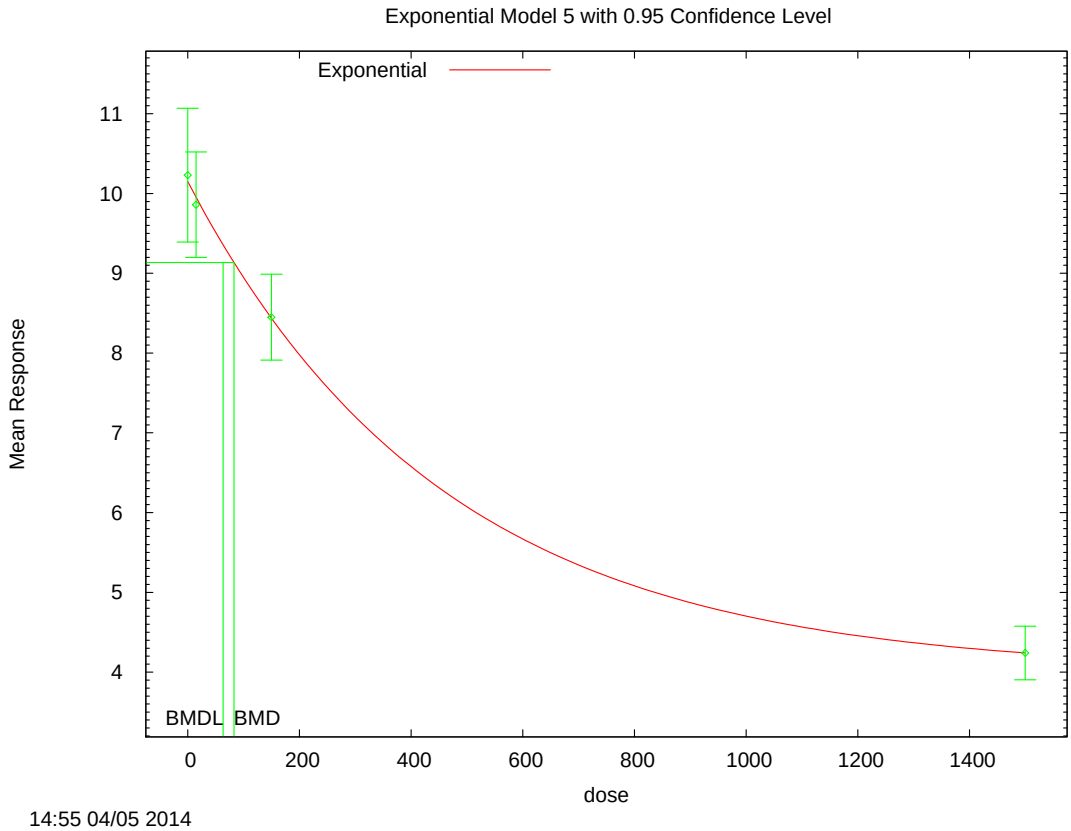

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MRID 43594101 - Acute Neurotoxicity Male Brainstem Day 1
CONSTANT VARIANCE - YES

```
 ================================================================
        Exponential Model. (Version: 1.7;  Date: 12/10/2009)
        Input Data File: C:/Users/EHolman/Desktop/HED Desktop/BMDS220/Data/exp_Acute
Neuro Male Brainstem Day 1_Setting.(d)
        Gnuplot Plotting File:
                                              Sat Apr 05 15:18:02 2014
 ================================================================

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 250
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha          -1.06264          -1.06264           -1.06264          -1.06264
         rho(S)              0                 0                  0                 0
           a           5.17069           5.17069             10.164            10.164
           b       0.000708074       0.000708074          0.00255075        0.00255075
           c                --                --               0.303593
0.303593
           d                --                 1                  --                 1

     (S) = Specified


                            Parameter Estimates by Model
```

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	-0.85993	-0.85993	-1.05185	-1.05185
rho	0	0	0	0
a	9.37106	9.37106	9.59991	9.59991
b	0.000732833	0.000732833	0.00188065	0.00188065
c	--	--	0.295608	0.295608
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	5	9.68	0.634
15	5	9.32	0.689
150	5	7.95	0.781
1500	5	3.24	0.491

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	9.371	0.6505	1.062
	15	9.269	0.6505	0.1766
	150	8.396	0.6505	-1.531
	1500	3.122	0.6505	0.4066
3	0	9.371	0.6505	1.062
	15	9.269	0.6505	0.1766
	150	8.396	0.6505	-1.531
	1500	3.122	0.6505	0.4066
4	0	9.6	0.591	0.303
	15	9.412	0.591	-0.3474
	150	7.938	0.591	0.0462
	1500	3.24	0.591	-0.001801
5	0	9.6	0.591	0.303
	15	9.412	0.591	-0.3474
	150	7.938	0.591	0.0462
	1500	3.24	0.591	-0.001801

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	0.6263587	5	8.747283

A2	1.164994	8	13.67001
A3	0.6263587	5	8.747283
R	-29.38312	2	62.76623
2	-1.400696	3	8.801393
3	-1.400696	3	8.801393
4	0.5184588	4	6.963082
5	0.5184588	4	6.963082

Additive constant for all log-likelihoods = -18.38. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	61.1	6	< 0.0001
Test 2	1.077	3	0.7826
Test 3	1.077	3	0.7826
Test 4	4.054	2	0.1317
Test 5a	4.054	2	0.1317
Test 5b	-2.265e-014	0	N/A
Test 6a	0.2158	1	0.6423
Test 6b	3.838	1	0.05009
Test 7a	0.2158	1	0.6423
Test 7b	3.838	1	0.05009
Test 7c	-2.542e-013	0	N/A

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is greater than .1. A homogeneous variance model appears to be appropriate here.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is greater than .1. Model 2 seems to adequately describe the data.

The p-value for Test 5a is greater than .1. Model 3 seems

to adequately describe the data.

Degrees of freedom for Test 5b are less than or equal to 0.
The Chi-Square test for fit is not valid.

The p-value for Test 6a is greater than .1. Model 4 seems
to adequately describe the data.

The p-value for Test 6b is greater than .05. Model 4 does
not seem to fit the data better than Model 2.

The p-value for Test 7a is greater than .1. Model 5 seems
to adequately describe the data.

The p-value for Test 7b is greater than .05. Model 5 does
not seem to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0.
The Chi-Square test for fit is not valid.

Benchmark Dose Computations:

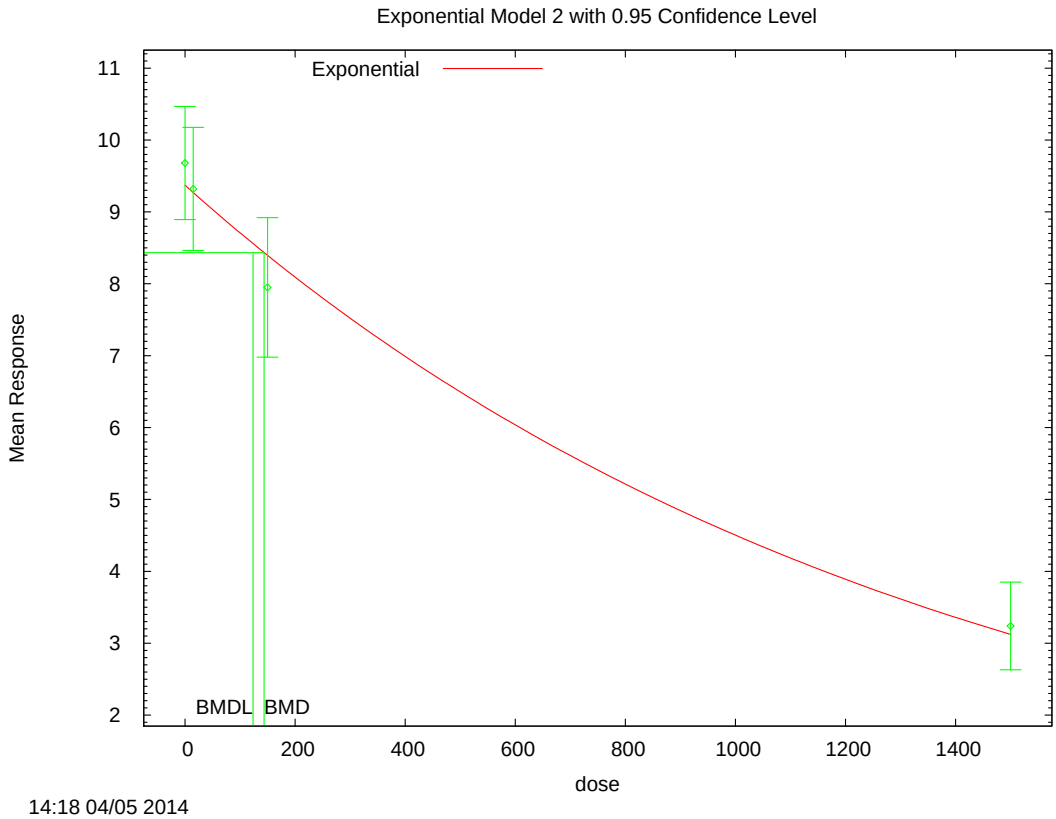
Specified Effect = 0.100000

Risk Type = Relative deviation

Confidence Level = 0.950000

BMD and BMDL by Model

Model	BMD	BMDL
2	143.772	123.608
3	143.772	123.608
4	81.4143	57.9696
5	81.4143	57.9696


Exponential Model 2 with 0.95 Confidence Level
Exponential
Mean Response
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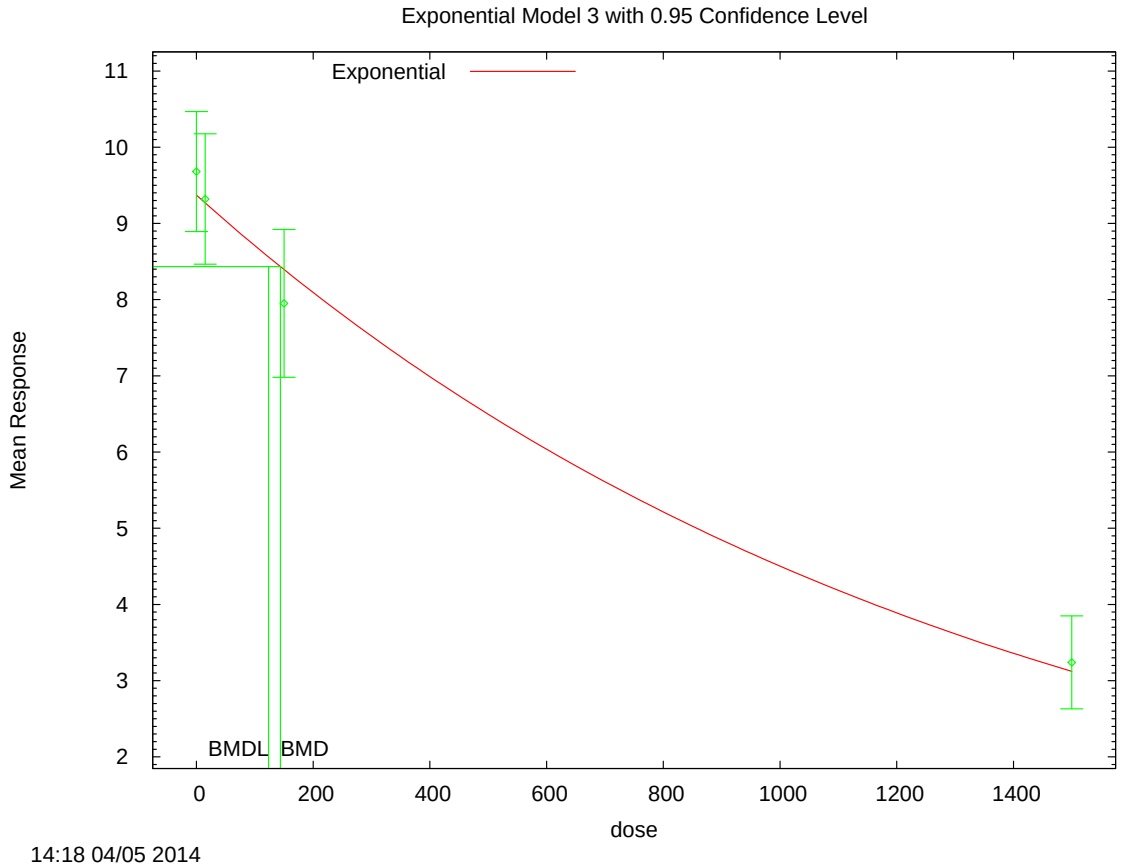
Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
dose
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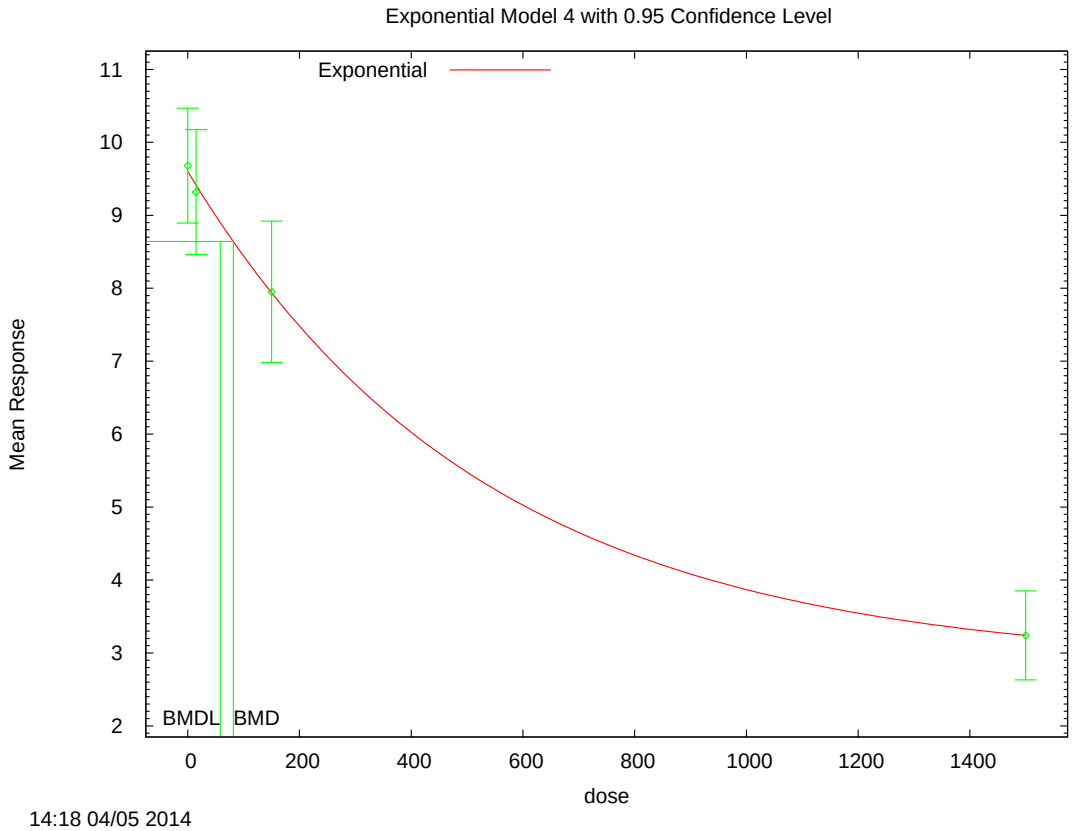

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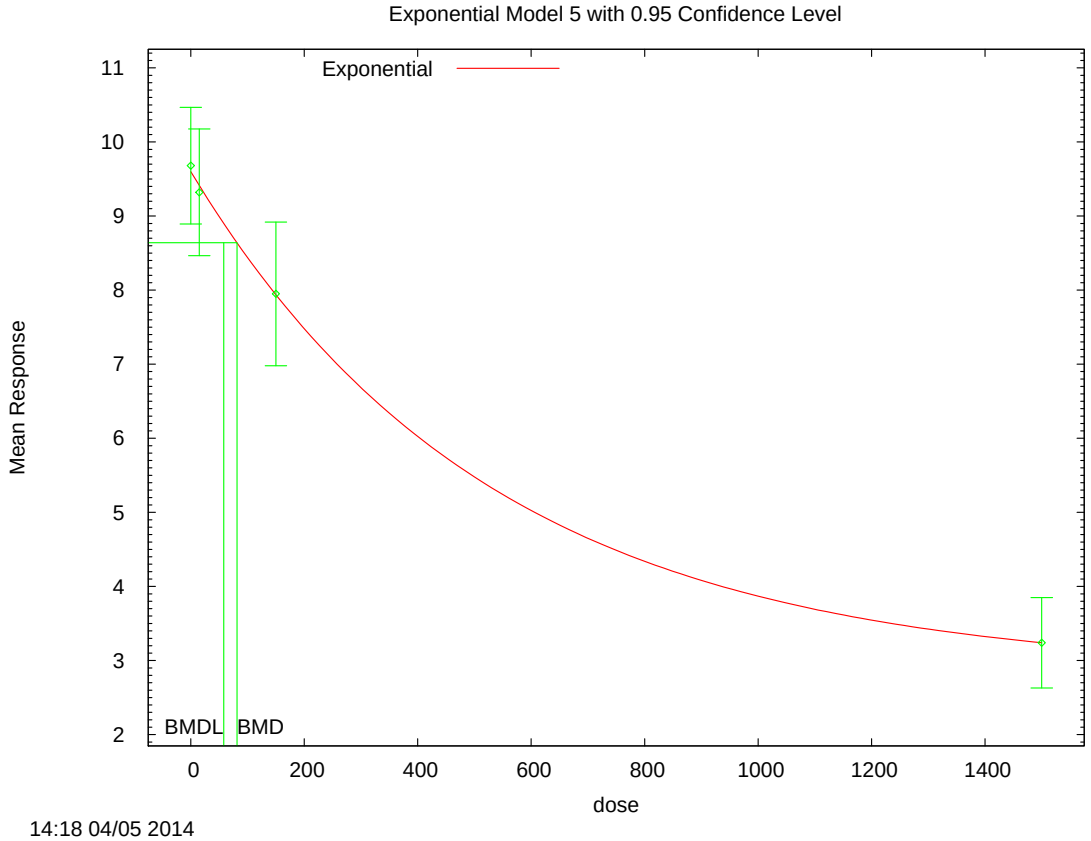

14:18 04/05 2014

MRID 43594101 - Acute Neurotoxicity Female Brainstem Day 1
CONSTANT VARIANCE - YES

```
 ================================================================
        Exponential Model. (Version: 1.7;  Date: 12/10/2009)
        Input Data File: C:/Users/EHolman/Desktop/HED Desktop/BMDS220/Data/exp_Acute
Neuro Female Brainstem Day 1_Setting.(d)
        Gnuplot Plotting File:
                                              Sat Apr 05 16:05:41 2014
 ================================================================

 BMDS Model Run
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   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 250
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha          -1.24538          -1.24538           -1.24538          -1.24538
         rho(S)              0                 0                  0                 0
           a           5.93303           5.93303            10.4475           10.4475
           b       0.000583921       0.000583921          0.00235929        0.00235929
           c                --                --               0.368281
0.368281
           d                --                 1                  --                 1

     (S) = Specified


                            Parameter Estimates by Model
```

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	-0.974502	-0.974502	-1.24535	-1.24535
rho	0	0	0	0
a	9.68989	9.68989	9.94618	9.94618
b	0.00060157	0.00060157	0.00197482	0.00197482
c	--	--	0.373812	0.373812
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	5	9.95	0.617
15	5	9.76	0.802
150	5	8.35	0.543
1500	5	4.04	0.347

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	9.69	0.6143	0.9468
	15	9.603	0.6143	0.572
	150	8.854	0.6143	-1.834
	1500	3.93	0.6143	0.3991
3	0	9.69	0.6143	0.9468
	15	9.603	0.6143	0.572
	150	8.854	0.6143	-1.834
	1500	3.93	0.6143	0.3991
4	0	9.946	0.5365	0.01594
	15	9.764	0.5365	-0.01829
	150	8.349	0.5365	0.002459
	1500	4.04	0.5365	-0.0001018
5	0	9.946	0.5365	0.01594
	15	9.764	0.5365	-0.01829
	150	8.349	0.5365	0.002459
	1500	4.04	0.5365	-0.0001018

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC

A1	2.453846	5	5.092309
A2	4.094482	8	7.811035
A3	2.453846	5	5.092309
R	-27.85617	2	59.71233
2	-0.254978	3	6.509956
3	-0.254978	3	6.509956
4	2.453548	4	3.092904
5	2.453548	4	3.092904

Additive constant for all log-likelihoods = -18.38. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	63.9	6	< 0.0001
Test 2	3.281	3	0.3503
Test 3	3.281	3	0.3503
Test 4	5.418	2	0.06662
Test 5a	5.418	2	0.06662
Test 5b	-4.708e-012	0	N/A
Test 6a	0.0005948	1	0.9805
Test 6b	5.417	1	0.01994
Test 7a	0.0005948	1	0.9805
Test 7b	5.417	1	0.01994
Test 7c	-8.882e-016	0	N/A

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is greater than .1. A homogeneous variance model appears to be appropriate here.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is less than .1. Model 2 may not adequately describe the data; you may want to consider another model.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Degrees of freedom for Test 5b are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

The p-value for Test 6b is less than .05. Model 4 appears to fit the data better than Model 2.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

The p-value for Test 7b is less than .05. Model 5 appears to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0. The Chi-Square test for fit is not valid.

Benchmark Dose Computations:

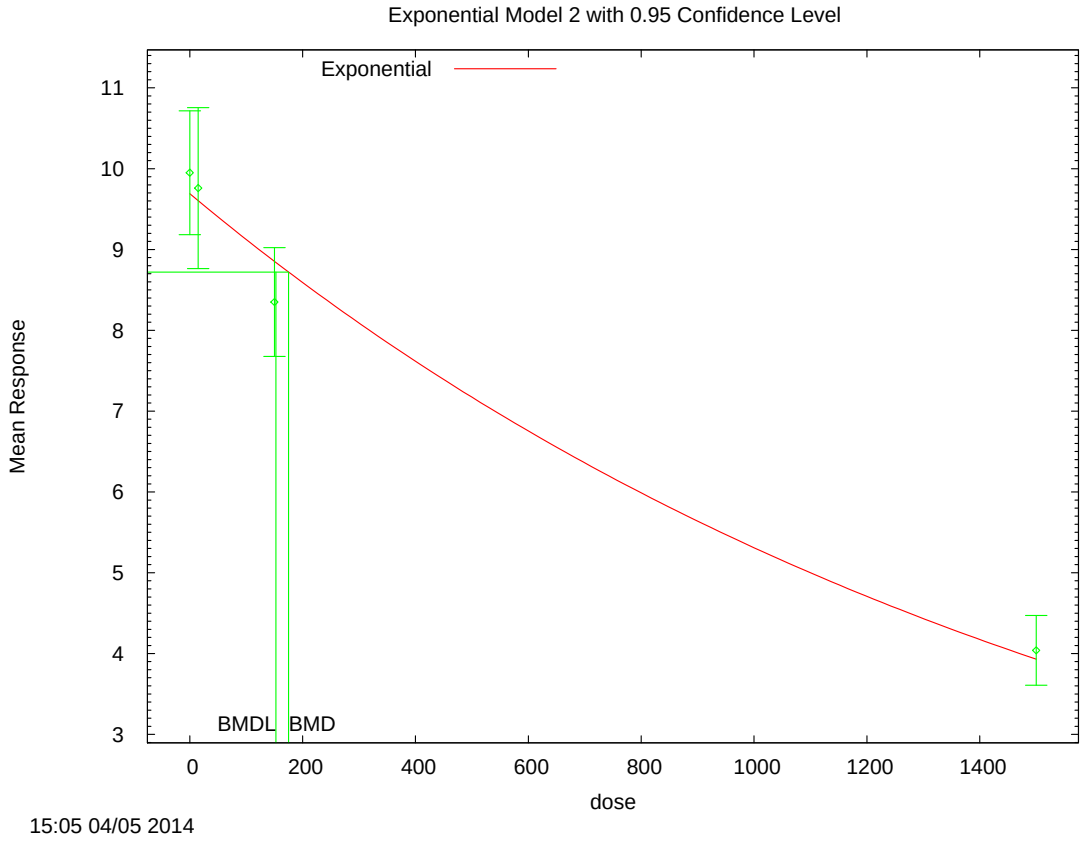
Specified Effect = 0.100000

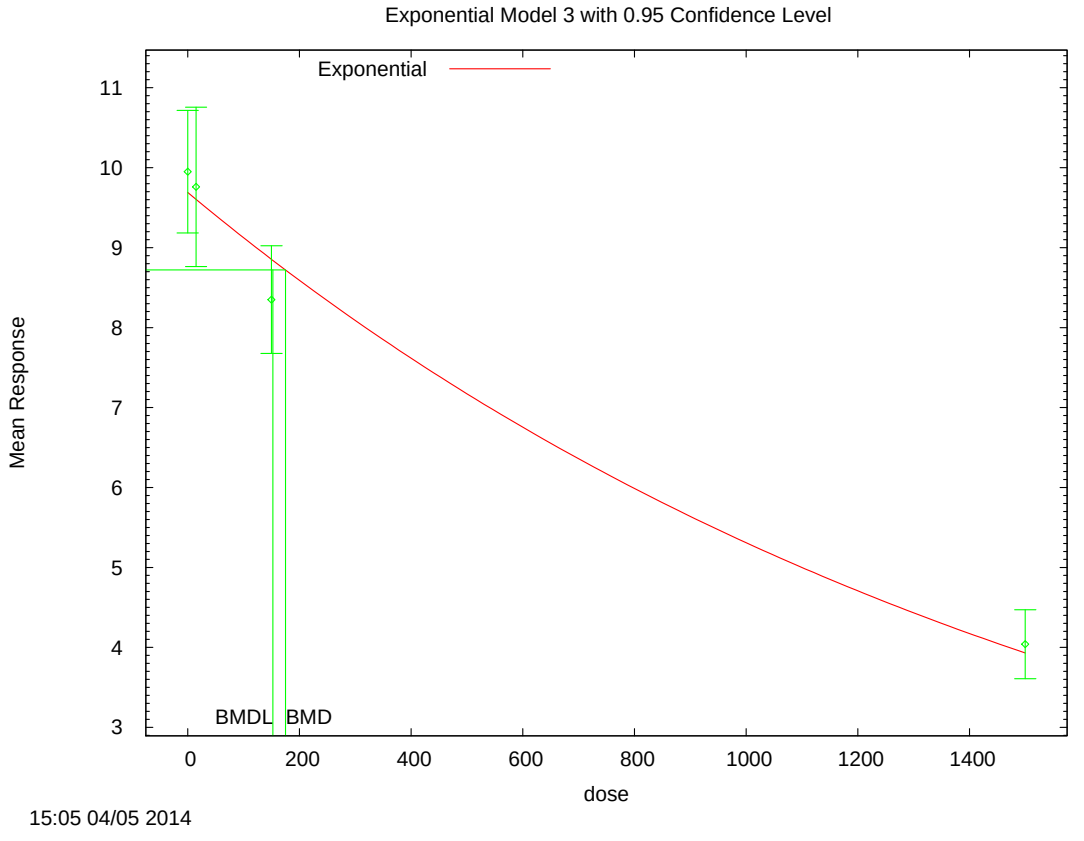
Risk Type = Relative deviation

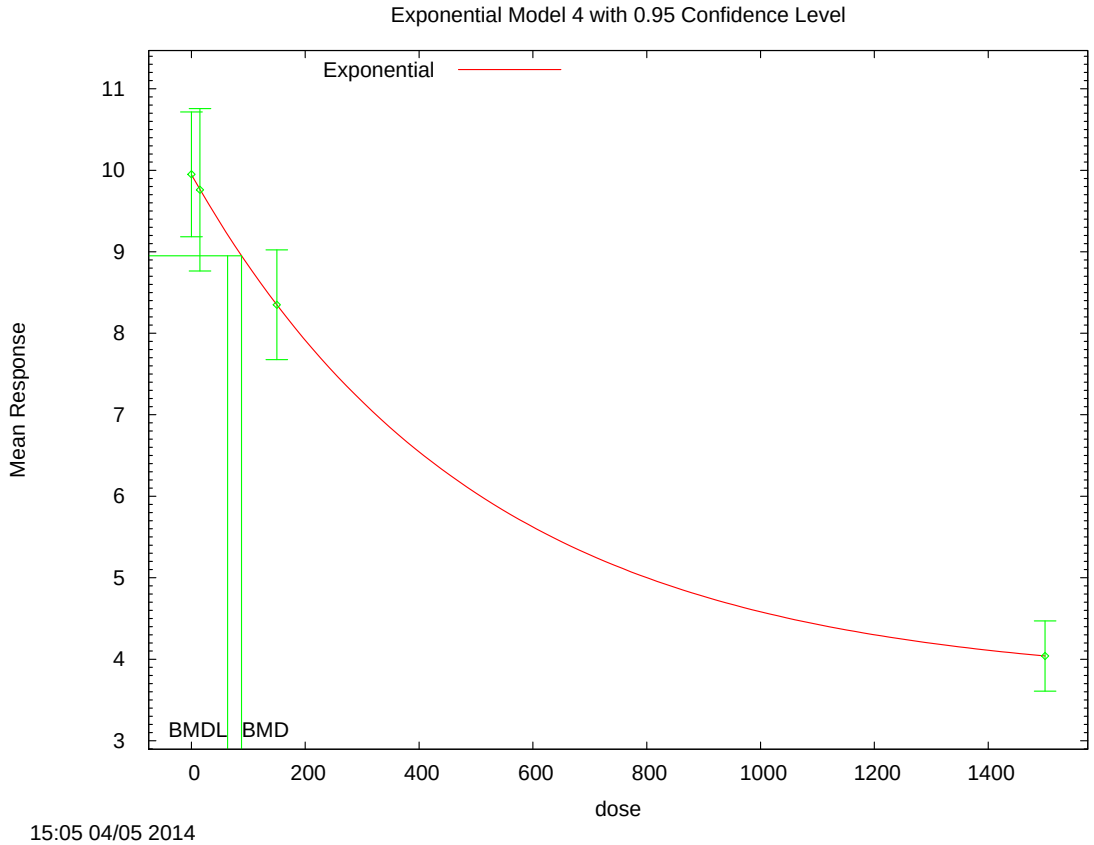
Confidence Level = 0.950000

BMD and BMDL by Model

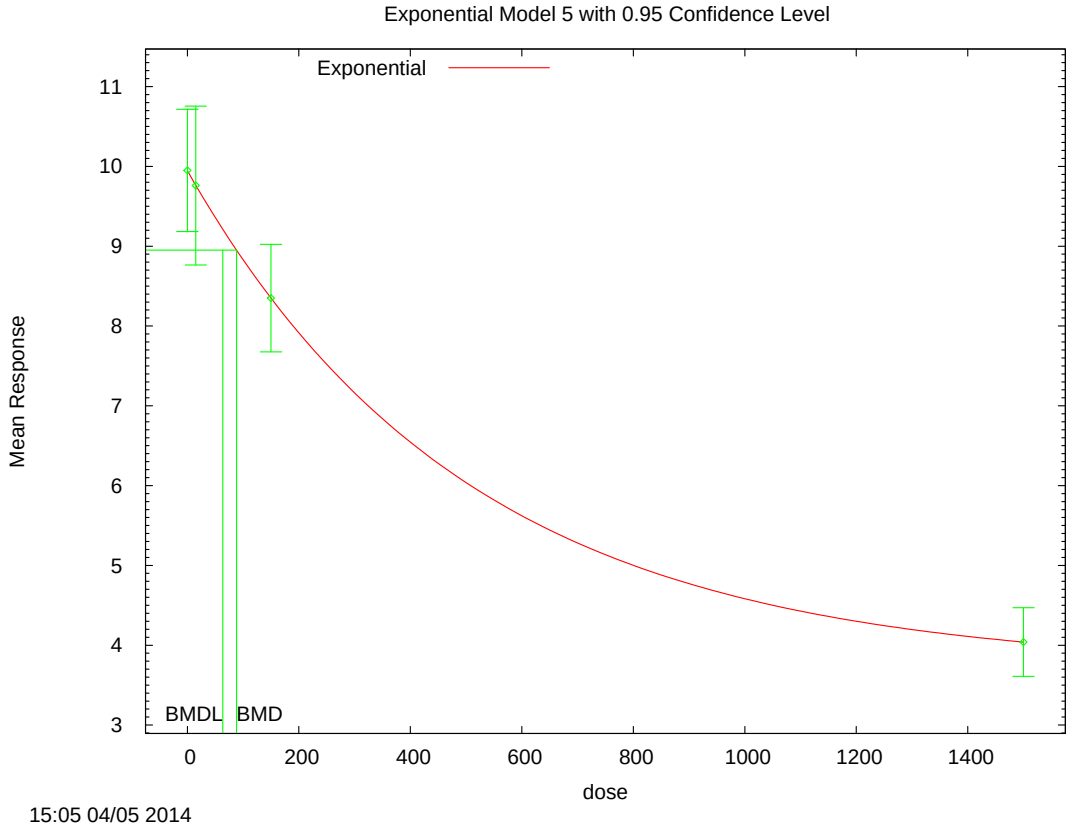
Model	BMD	BMDL
2	175.143	152.596
3	175.143	152.596
4	88.1055	63.5833
5	88.1055	63.5833


Exponential Model 2 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
11
10
9
8
7
6
5
4
3
0
200
400
600
800
1000
1200
1400
15:05 04/05 2014


Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
11
10
9
8
7
6
5
4
3
0
200
400
600
800
1000
1200
1400
15:05 04/05 2014



15:05 04/05 2014



15:05 04/05 2014

MRID 43594101 - Acute Neurotoxicity Male Cerebellum Day 1
CONSTANT VARIANCE - YES

```
 ================================================================
        Exponential Model. (Version: 1.7;  Date: 12/10/2009)
        Input Data File: C:/Users/EHolman/Desktop/HED Desktop/BMDS220/Data/exp_Acute
Neuro Male Cerebellum Day 1_Setting.(d)
        Gnuplot Plotting File:
                                            Sat Apr 05 15:26:15 2014
 ================================================================

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 250
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha          -3.03755          -3.03755           -3.03755          -3.03755
         rho(S)              0                 0                  0                 0
           a           2.06353           2.06353             4.6095            4.6095
           b       0.000795019       0.000795019          0.00272708        0.00272708
           c                --                --               0.254134
0.254134
           d                --                 1                  --                 1

     (S) = Specified


                           Parameter Estimates by Model
```

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	-2.01148	-2.01148	-2.96539	-2.96539
rho	0	0	0	0
a	4.07279	4.07279	4.31271	4.31271
b	0.000886272	0.000886273	0.00335702	0.00335702
c	--	--	0.280816	0.280816
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	5	4.39	0.242
15	5	4.07	0.299
150	5	3.1	0.286
1500	5	1.23	0.1

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	4.073	0.3658	1.939
	15	4.019	0.3658	0.3118
	150	3.566	0.3658	-2.848
	1500	1.078	0.3658	0.9305
3	0	4.073	0.3658	1.939
	15	4.019	0.3658	0.3118
	150	3.566	0.3658	-2.848
	1500	1.078	0.3658	0.9305
4	0	4.313	0.227	0.7612
	15	4.16	0.227	-0.8903
	150	3.086	0.227	0.1414
	1500	1.231	0.227	-0.0123
5	0	4.313	0.227	0.7612
	15	4.16	0.227	-0.8903
	150	3.086	0.227	0.1414
	1500	1.231	0.227	-0.0123

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	20.37551	5	-30.75101

A2	23.13382	8	-30.26765
A3	20.37551	5	-30.75101
R	-14.47196	2	32.94392
2	10.11478	3	-14.22955
3	10.11478	3	-14.22955
4	19.65391	4	-31.30782
5	19.65391	4	-31.30782

Additive constant for all log-likelihoods = -18.38. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	75.21	6	< 0.0001
Test 2	5.517	3	0.1376
Test 3	5.517	3	0.1376
Test 4	20.52	2	< 0.0001
Test 5a	20.52	2	< 0.0001
Test 5b	-3.513e-011	0	N/A
Test 6a	1.443	1	0.2296
Test 6b	19.08	1	< 0.0001
Test 7a	1.443	1	0.2296
Test 7b	19.08	1	< 0.0001
Test 7c	-1.066e-013	0	N/A

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is greater than .1. A homogeneous variance model appears to be appropriate here.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is less than .1. Model 2 may not adequately describe the data; you may want to consider another model.

The p-value for Test 5a is less than .1. Model 3 may not adequately

describe the data; you may want to consider another model.

Degrees of freedom for Test 5b are less than or equal to 0.
The Chi-Square test for fit is not valid.

The p-value for Test 6a is greater than .1. Model 4 seems
to adequately describe the data.

The p-value for Test 6b is less than .05. Model 4 appears
to fit the data better than Model 2.

The p-value for Test 7a is greater than .1. Model 5 seems
to adequately describe the data.

The p-value for Test 7b is less than .05. Model 5 appears
to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0.
The Chi-Square test for fit is not valid.

Benchmark Dose Computations:

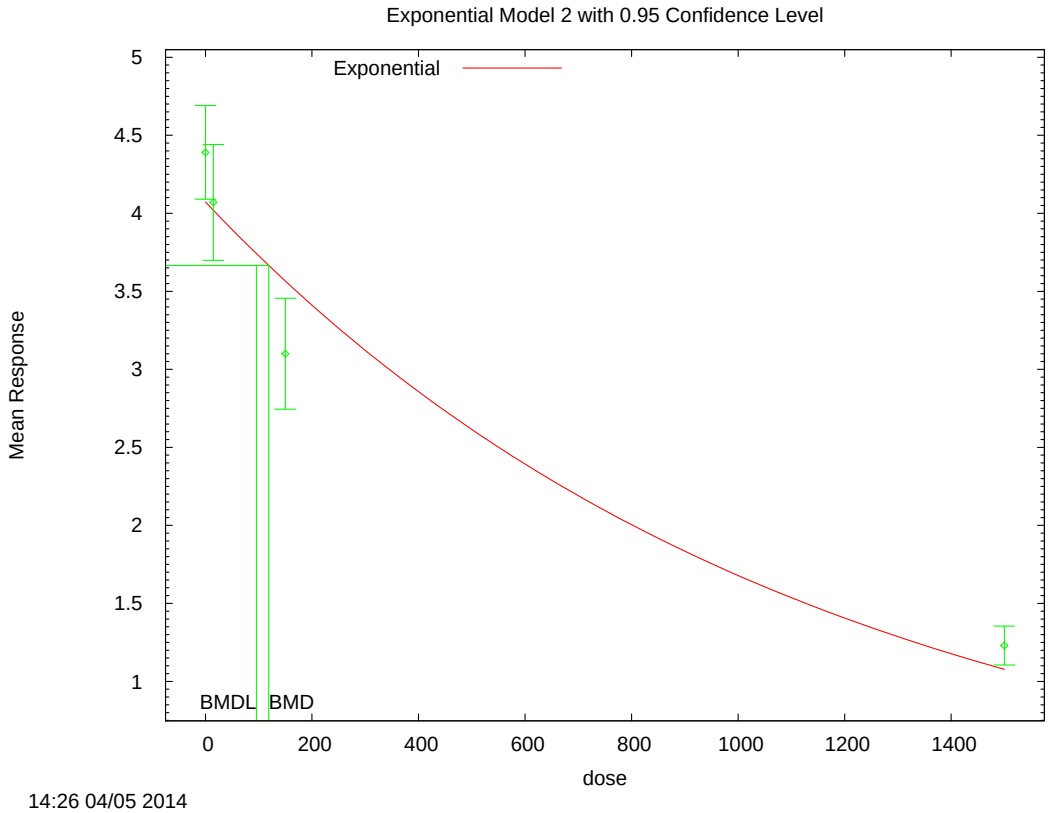
Specified Effect = 0.100000

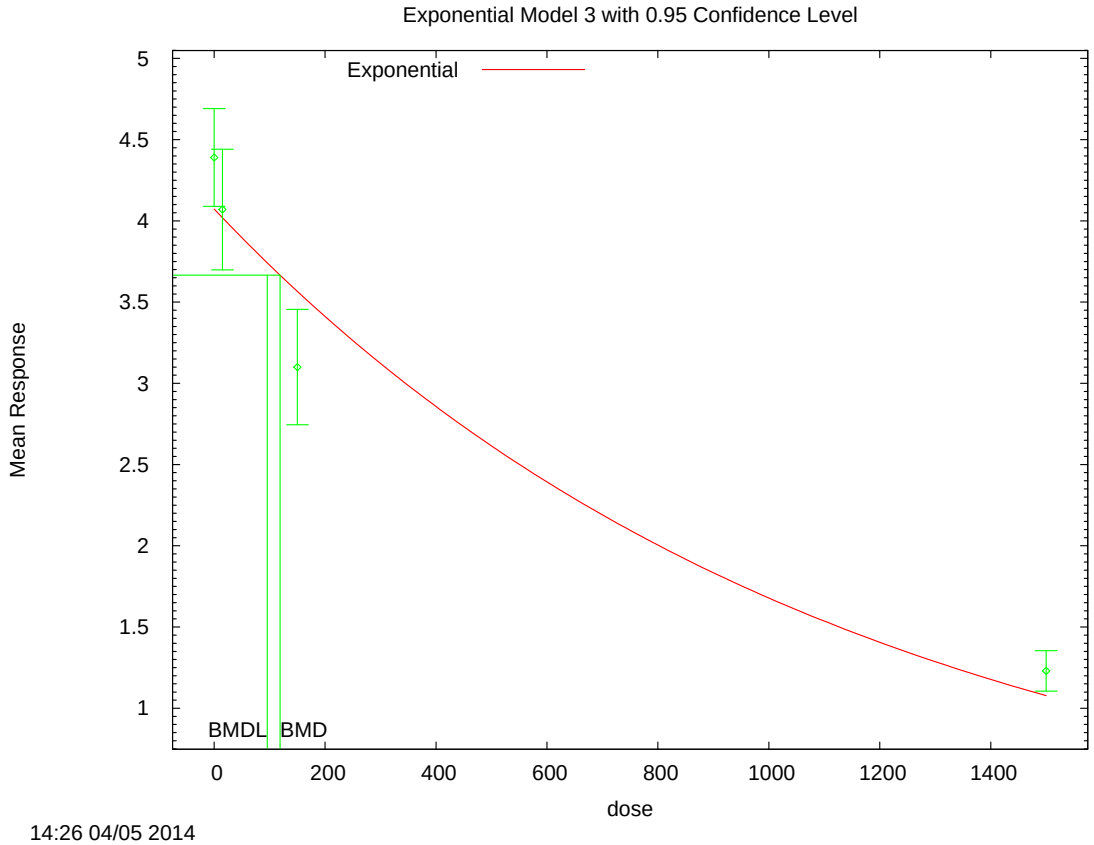
Risk Type = Relative deviation

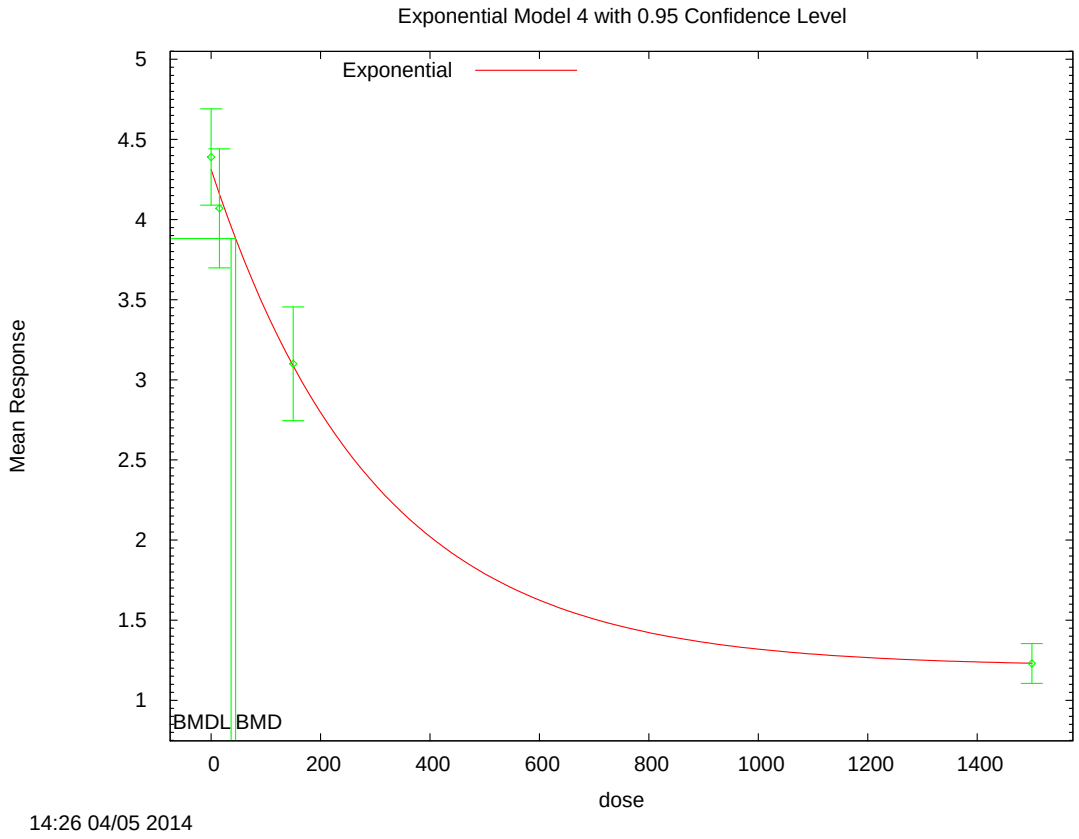
Confidence Level = 0.950000

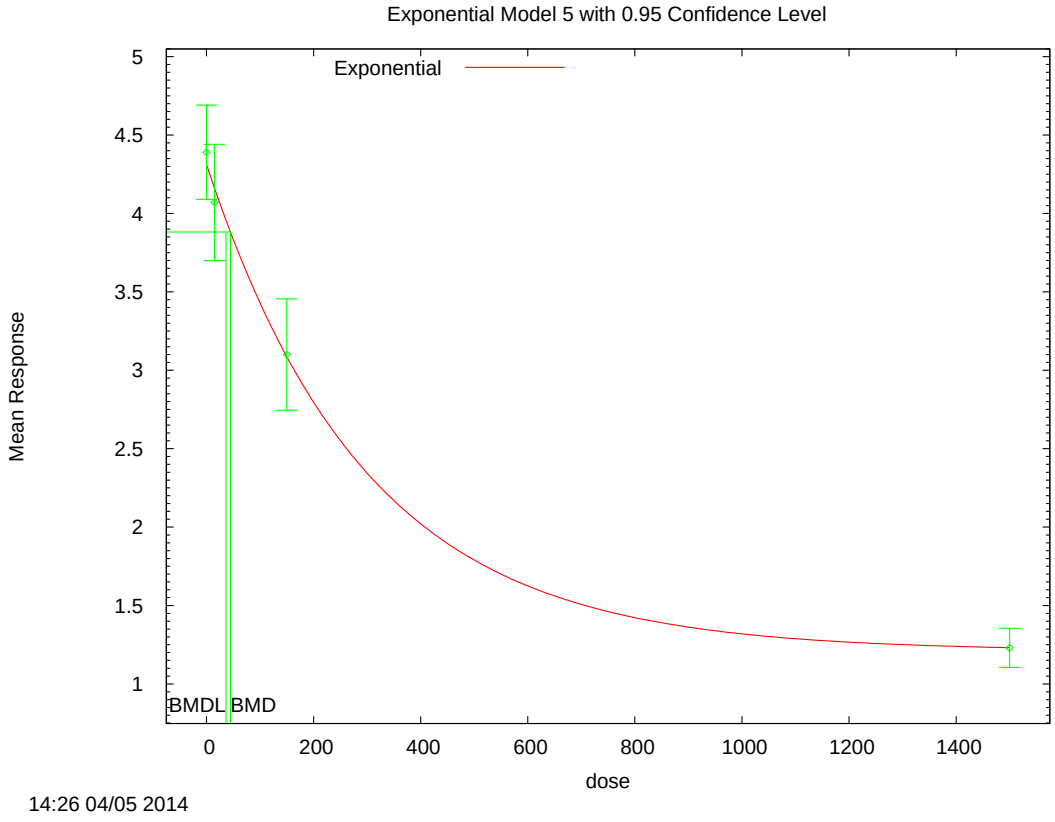
BMD and BMDL by Model

Model	BMD	BMDL
2	118.881	95.642
3	118.88	95.642
4	44.5976	36.3501
5	44.5976	36.3501


Exponential Model 2 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
5
4.5
4
3.5
3
2.5
2
1.5
1
0
200
400
600
800
1000
1200
1400
14:26 04/05 2014


Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
5
4.5
4
3.5
3
2.5
2
1.5
1
0
200
400
600
800
1000
1200
1400
14:26 04/05 2014


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL BMD
5
4.5
4
3.5
3
2.5
2
1.5
1
0
200
400
600
800
1000
1200
1400
14:26 04/05 2014


Exponential Model 5 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL BMD
5
4.5
4
3.5
3
2.5
2
1.5
1
0
200
400
600
800
1000
1200
1400
14:26 04/05 2014

MRID 43594101 - Acute Neurotoxicity Female Cerebellum Day 1
CONSTANT VARIANCE - YES

```
 ================================================================
        Exponential Model. (Version: 1.7;  Date: 12/10/2009)
        Input Data File: C:/Users/EHolman/Desktop/HED Desktop/BMDS220/Data/exp_Acute
Neuro Female Cerebellum Day 1_Setting.(d)
        Gnuplot Plotting File:
                                              Sat Apr 05 16:14:34 2014
 ================================================================

 BMDS Model Run
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   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 250
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha          -3.47274          -3.47274           -3.47274          -3.47274
         rho(S)              0                 0                  0                 0
           a           2.24401           2.24401            4.3785            4.3785
           b       0.000645232       0.000645232         0.00251093        0.00251093
           c                --                --               0.321919
0.321919
           d                --                 1                  --                 1

     (S) = Specified
```

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	-2.09099	-2.09099	-3.47219	-3.47219
rho	0	0	0	0
a	3.90263	3.90263	4.16471	4.16471
b	0.000706806	0.000706806	0.00377957	0.00377957
c	--	--	0.353162	0.353162
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	5	4.17	0.246
15	5	4.01	0.172
150	5	3	0.224
1500	5	1.48	0.122

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	3.903	0.3515	1.701
	15	3.861	0.3515	0.9448
	150	3.51	0.3515	-3.245
	1500	1.352	0.3515	0.8155
3	0	3.903	0.3515	1.701
	15	3.861	0.3515	0.9448
	150	3.51	0.3515	-3.245
	1500	1.352	0.3515	0.8155
4	0	4.165	0.1762	0.06718
	15	4.016	0.1762	-0.07904
	150	2.999	0.1762	0.01325
	1500	1.48	0.1762	-0.001382
5	0	4.165	0.1762	0.06718
	15	4.016	0.1762	-0.07904
	150	2.999	0.1762	0.01325
	1500	1.48	0.1762	-0.001382

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC

A1	24.72736	5	-39.45473
A2	26.04408	8	-36.08815
A3	24.72736	5	-39.45473
R	-11.64376	2	27.28751
2	10.90992	3	-15.81984
3	10.90992	3	-15.81984
4	24.72189	4	-41.44379
5	24.72189	4	-41.44379

Additive constant for all log-likelihoods = -18.38. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	75.38	6	< 0.0001
Test 2	2.633	3	0.4517
Test 3	2.633	3	0.4517
Test 4	27.63	2	< 0.0001
Test 5a	27.63	2	< 0.0001
Test 5b	-3.265e-012	0	N/A
Test 6a	0.01094	1	0.9167
Test 6b	27.62	1	< 0.0001
Test 7a	0.01094	1	0.9167
Test 7b	27.62	1	< 0.0001
Test 7c	7.105e-015	0	N/A

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is greater than .1. A homogeneous variance model appears to be appropriate here.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is less than .1. Model 2 may not adequately describe the data; you may want to consider another model.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Degrees of freedom for Test 5b are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

The p-value for Test 6b is less than .05. Model 4 appears to fit the data better than Model 2.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

The p-value for Test 7b is less than .05. Model 5 appears to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0. The Chi-Square test for fit is not valid.

Benchmark Dose Computations:

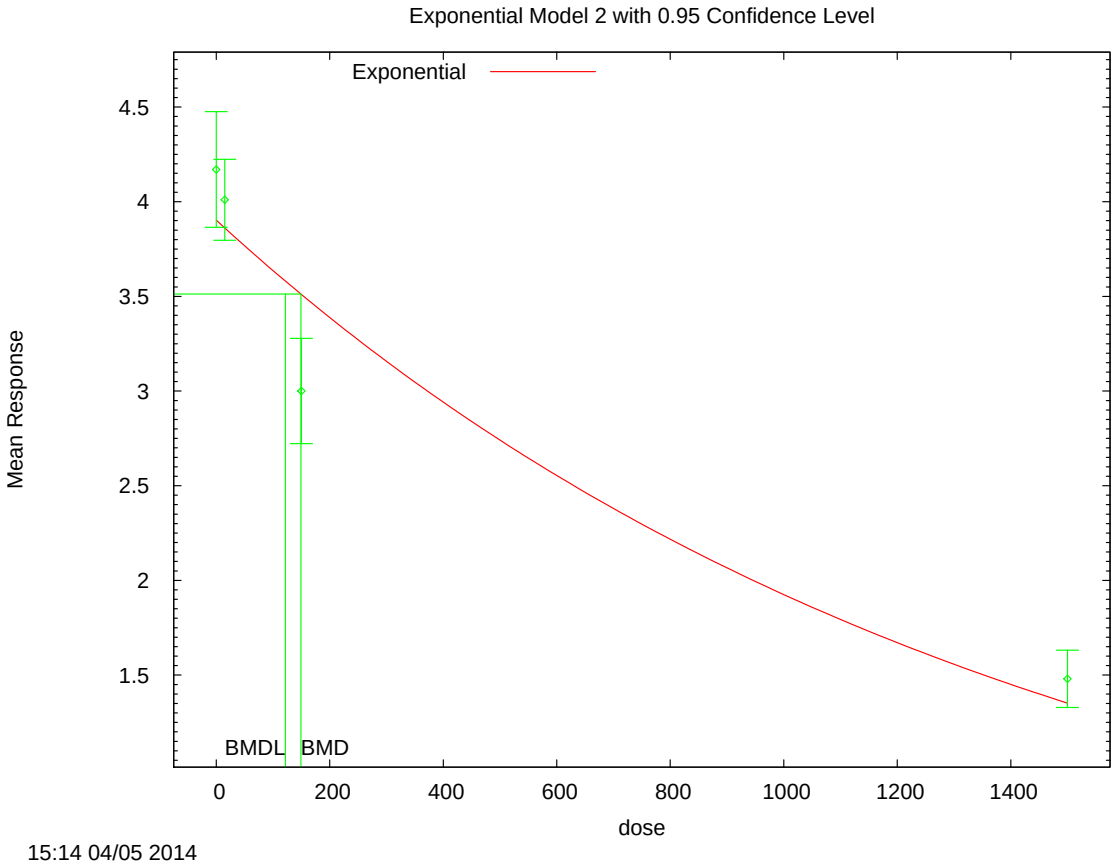
Specified Effect = 0.100000

Risk Type = Relative deviation

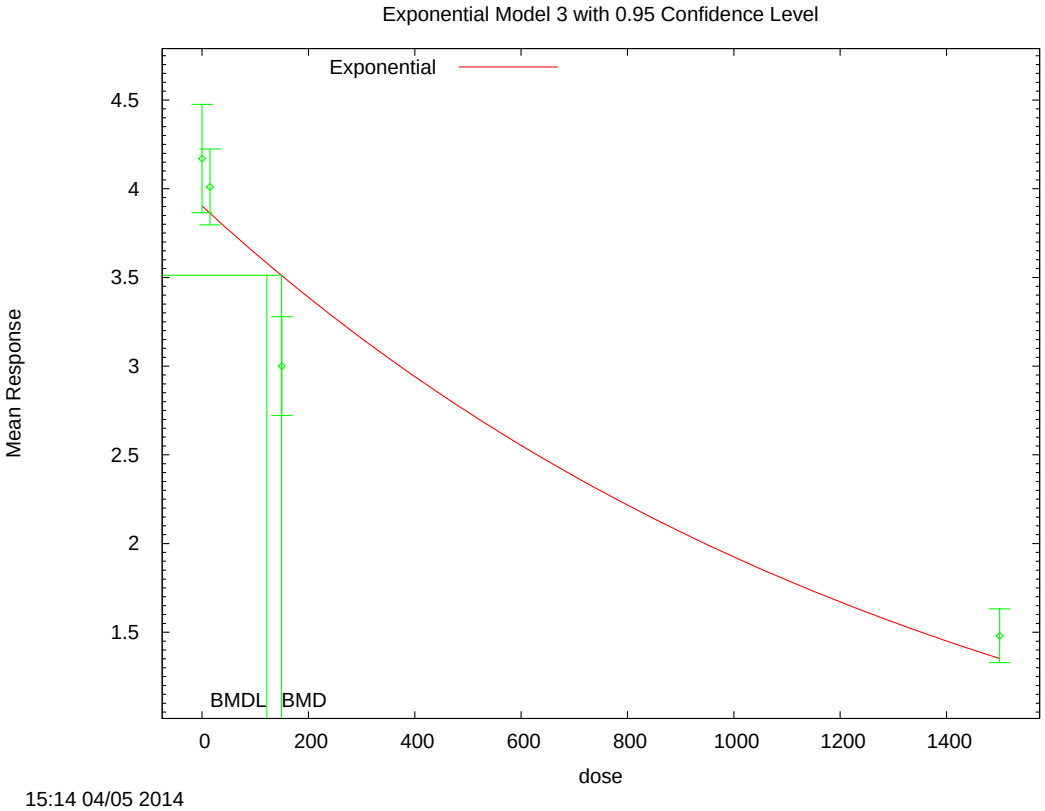
Confidence Level = 0.950000

BMD and BMDL by Model

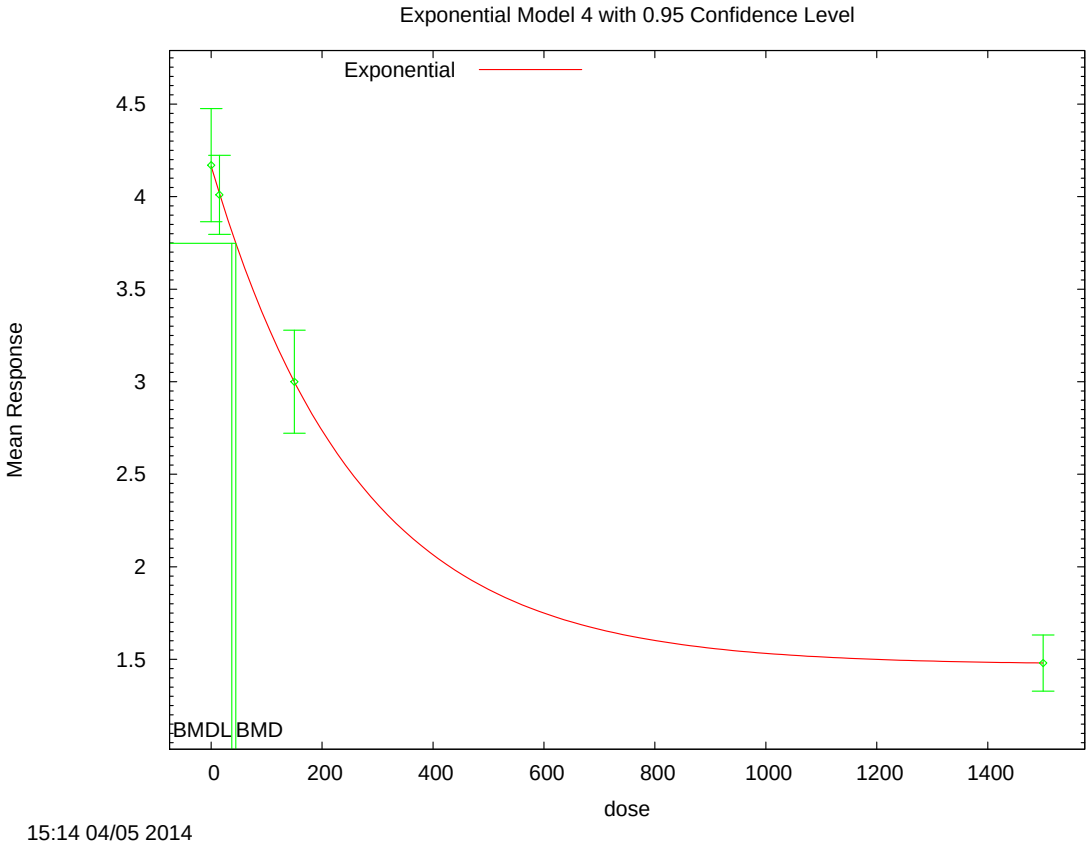
Model	BMD	BMDL
2	149.066	121.743
3	149.066	121.743
4	44.4345	37.3193
5	44.4345	37.3193

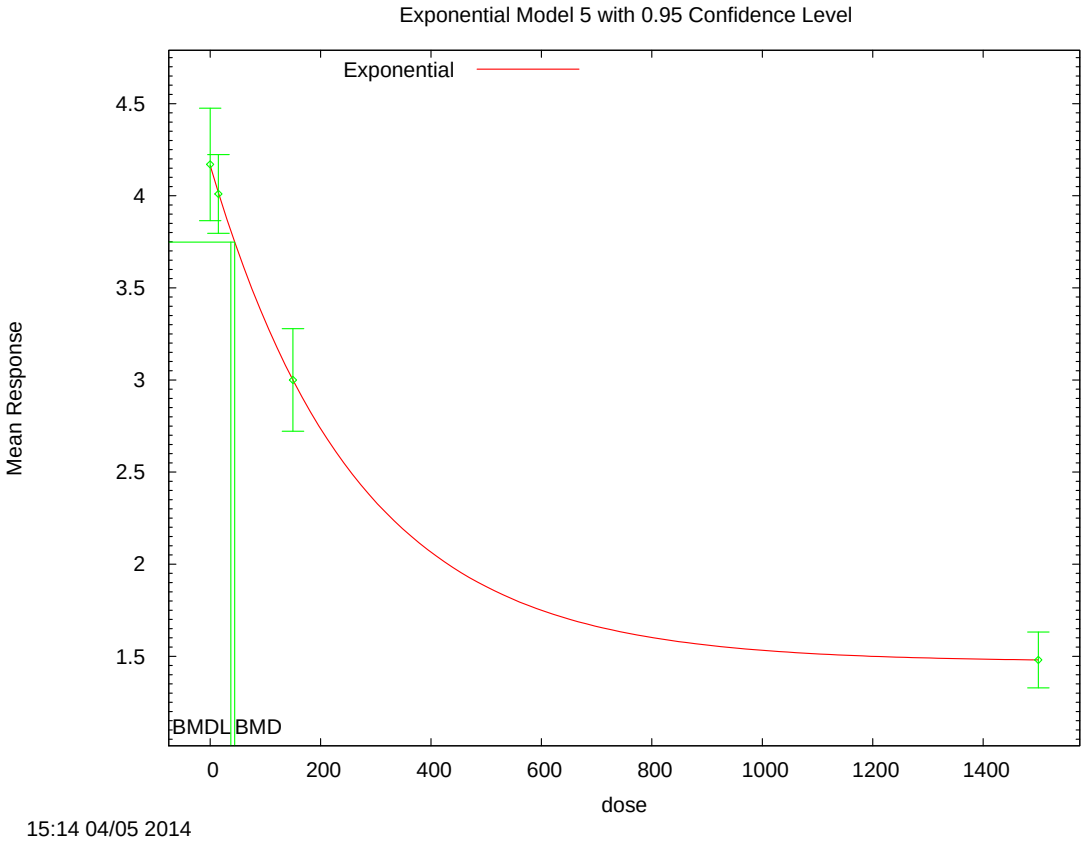


15:14 04/05 2014



15:14 04/05 2014


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL BMD
4.5
4
3.5
3
2.5
2
1.5
0
200
400
600
800
1000
1200
1400
15:14 04/05 2014


Exponential Model 5 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL BMD
4.5
4
3.5
3
2.5
2
1.5
0
200
400
600
800
1000
1200
1400
15:14 04/05 2014

MRID 49037406 - Repeat CCA Male Adult RBC ChE - Constant Variance - YES

```
 ================================================================
        Exponential Model. (Version: 1.9;  Date: 01/29/2013)
        Input Data File: F:/Pirimiphos-methyl/BMD runs/exp_Repeat CCA Adult Male
RBC_Setting.(d)
        Gnuplot Plotting File:
                                              Tue Apr 01 11:42:29 2014
 ================================================================

 BMDS Model Run
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   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha           -4.1837           -4.1837             -4.1837           -4.1837
         rho(S)              0                 0                   0                 0
           a          0.573788          0.805772            1.48155           1.48155
           b         0.0304791       0.000908741          0.0496258         0.0496258
           c                --                --               0.191691
0.191691
           d                --                 2                  --                 1

     (S) = Specified


                               Parameter Estimates by Model

     Variable          Model 2           Model 3           Model 4           Model 5
```

lnalpha	-4.12898	-4.12898	-4.18219	-4.1837
rho	0	0	0	0
a	1.38946	1.38946	1.41274	1.411
b	0.0320715	0.0320715	0.0549594	0.0633464
c	--	--	0.256683	0.310989
d	--	1	--	1.09371

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	1.411	0.131
7.5	10	1.063	0.13
20	9	0.705	0.128
30	10	0.568	0.132

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	1.389	0.1269	0.5368
	7.5	1.092	0.1269	-0.7328
	20	0.7316	0.1269	-0.6291
	30	0.5309	0.1269	0.9253
3	0	1.389	0.1269	0.5368
	7.5	1.092	0.1269	-0.7328
	20	0.7316	0.1269	-0.6291
	30	0.5309	0.1269	0.9253
4	0	1.413	0.1236	-0.04443
	7.5	1.058	0.1236	0.1279
	20	0.7125	0.1236	-0.1812
	30	0.5645	0.1236	0.08842
5	0	1.411	0.1235	1.828e-007
	7.5	1.063	0.1235	-4.661e-007
	20	0.705	0.1235	1.604e-006
	30	0.568	0.1235	-1.224e-006

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	62.08219	5	-114.1644
A2	62.08928	8	-108.1786

A3	62.08219	5	-114.1644
R	21.17061	2	-38.34122
2	61.01503	3	-116.0301
3	61.01503	3	-116.0301
4	62.05269	4	-116.1054
5	62.08219	5	-114.1644

Additive constant for all log-likelihoods = -35.84. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	81.84	6	< 0.0001
Test 2	0.01417	3	0.9996
Test 3	0.01417	3	0.9996
Test 4	2.134	2	0.344
Test 5a	2.134	2	0.344
Test 5b	-1.127e-011	0	N/A
Test 6a	0.05901	1	0.8081
Test 6b	2.075	1	0.1497
Test 7a	4.32e-012	0	N/A
Test 7b	2.134	2	0.344
Test 7c	0.05901	1	0.8081

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is greater than .1. A homogeneous variance model appears to be appropriate here.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is greater than .1. Model 2 seems to adequately describe the data.

The p-value for Test 5a is greater than .1. Model 3 seems to adequately describe the data.

Degrees of freedom for Test 5b are less than or equal to 0.
The Chi-Square test for fit is not valid.

The p-value for Test 6a is greater than .1. Model 4 seems
to adequately describe the data.

The p-value for Test 6b is greater than .05. Model 4 does
not seem to fit the data better than Model 2.

Degrees of freedom for Test 7a are less than or equal to 0.
The Chi-Square test for fit is not valid.

The p-value for Test 7b is greater than .05. Model 5 does
not seem to fit the data better than Model 3.

The p-value for Test 7c is greater than .05. Model 5 does
not seem to fit the data better than Model 4.

Benchmark Dose Computations:

Specified Effect = 0.100000

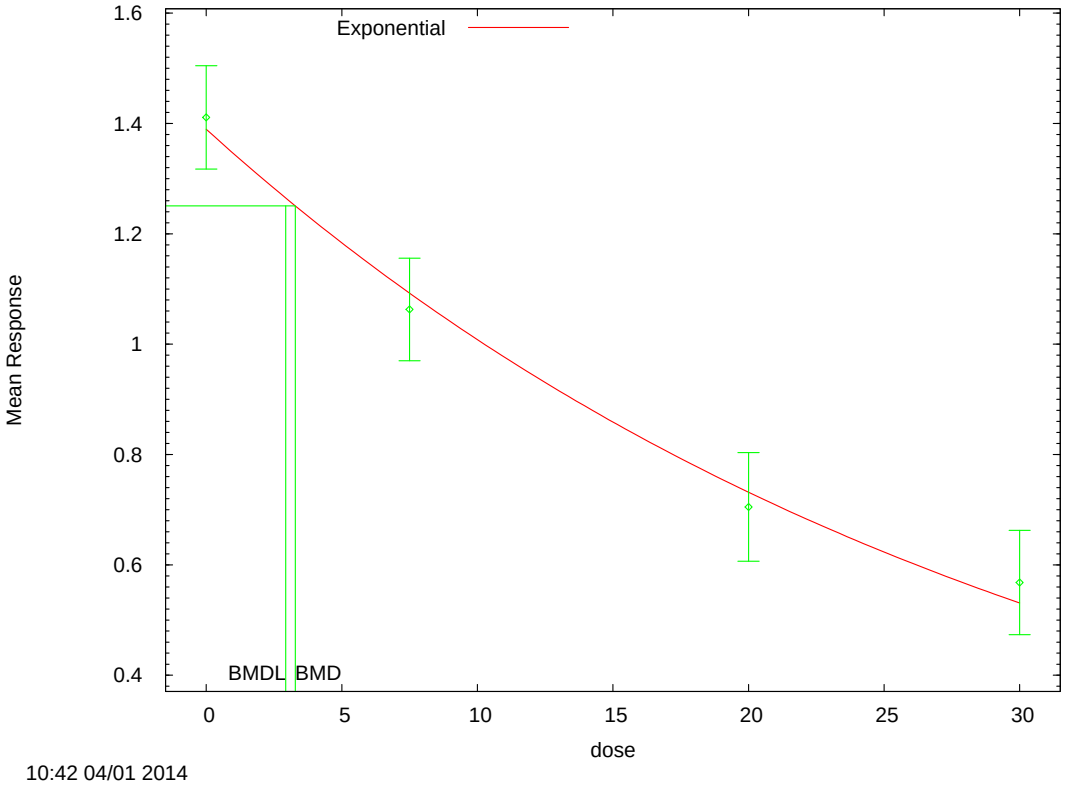
Risk Type = Relative deviation

Confidence Level = 0.950000

BMD and BMDL by Model

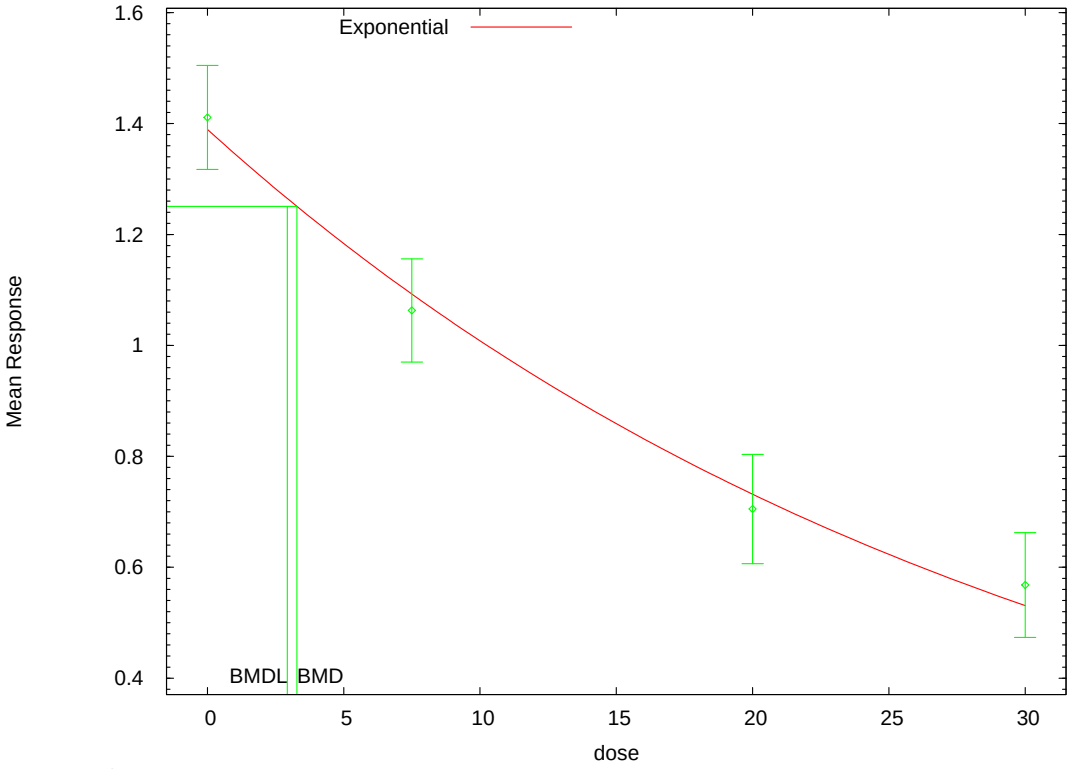
Model	BMD	BMDL
2	3.28518	2.93175
3	3.28518	2.93175
4	2.62894	2.02629
5	2.90132	2.0321

Exponential Model 2, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



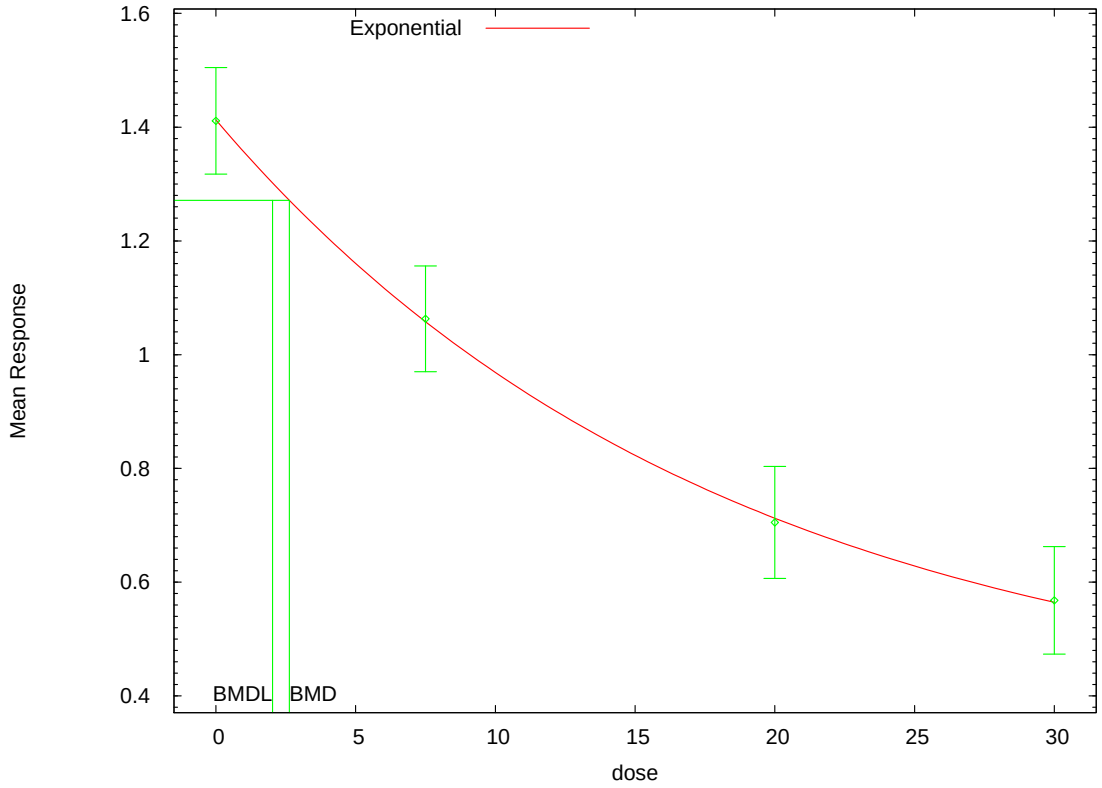
10:42 04/01 2014

Exponential Model 3, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



10:42 04/01 2014

Exponential Model 4, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



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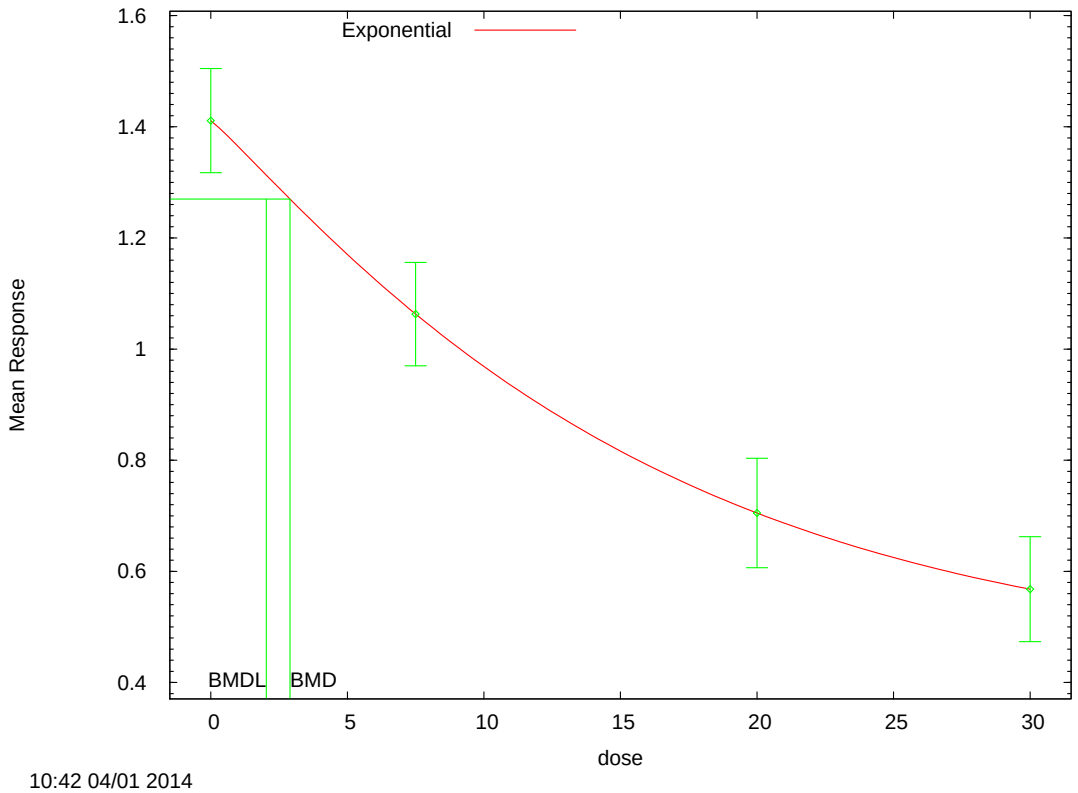
Exponential Model 5, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



10:42 04/01 2014

MRID 49037406 - Repeat CCA Female Adult RBC ChE - Non-Constant Variance - YES

```
 ================================================================
        Exponential Model. (Version: 1.9;  Date: 01/29/2013)
        Input Data File: F:/Pirimiphos-methyl/BMD runs/exp_Repeat CCA Adult Female
RBC_Setting.(d)
        Gnuplot Plotting File:
                                                Tue Apr 01 12:08:01 2014
 ================================================================

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log(mean(i)) * rho)

   Total number of dose groups = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                              Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha          -4.15643          -4.15643           -4.15643          -4.15643
         rho           0.32906           0.32906            0.32906           0.32906
           a          0.434454          0.690303            1.42275           1.42275
           b         0.0354475        0.00121285           0.116891          0.116891
           c                --                --               0.300558
0.300558
           d                --                 2                    --                 1


                            Parameter Estimates by Model

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha       -3.76468          -3.76468           -4.21813          -4.21813
```

rho	0.458999	0.459	-0.338367	-0.338366
a	1.28383	1.28383	1.35259	1.35259
b	0.0386629	0.0386629	0.095245	0.095245
c	--	--	0.307234	0.307234
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	9	1.355	0.111
7.5	10	0.864	0.133
20	10	0.583	0.19
30	10	0.449	0.072

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	1.284	0.1612	1.324
	7.5	0.9607	0.1508	-2.027
	20	0.5925	0.135	-0.2224
	30	0.4025	0.1235	1.19
3	0	1.284	0.1612	1.324
	7.5	0.9607	0.1508	-2.027
	20	0.5925	0.135	-0.2224
	30	0.4025	0.1235	1.19
4	0	1.353	0.1153	0.06264
	7.5	0.8743	0.1241	-0.2612
	20	0.555	0.1341	0.6598
	30	0.4694	0.1379	-0.467
5	0	1.353	0.1153	0.06264
	7.5	0.8743	0.1241	-0.2612
	20	0.555	0.1341	0.6598
	30	0.4694	0.1379	-0.467

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	60.97005	5	-111.9401
A2	65.48672	8	-114.9734
A3	60.99577	6	-109.9915
R	19.9966	2	-35.9932

2	56.77699	4	-105.554
3	56.77699	4	-105.554
4	60.71036	5	-111.4207
5	60.71036	5	-111.4207

Additive constant for all log-likelihoods = -35.84. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	90.98	6	< 0.0001
Test 2	9.033	3	0.02885
Test 3	8.982	2	0.01121
Test 4	8.438	2	0.01472
Test 5a	8.438	2	0.01472
Test 5b	-1.535e-012	0	N/A
Test 6a	0.5708	1	0.4499
Test 6b	7.867	1	0.005035
Test 7a	0.5708	1	0.4499
Test 7b	7.867	1	0.005035
Test 7c	-5.542e-013	0	N/A

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 4 is less than .1. Model 2 may not adequately describe the data; you may want to consider another model.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Degrees of freedom for Test 5b are less than or equal to 0.

The Chi-Square test for fit is not valid.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

The p-value for Test 6b is less than .05. Model 4 appears to fit the data better than Model 2.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

The p-value for Test 7b is less than .05. Model 5 appears to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0. The Chi-Square test for fit is not valid.

Benchmark Dose Computations:

Specified Effect = 0.100000

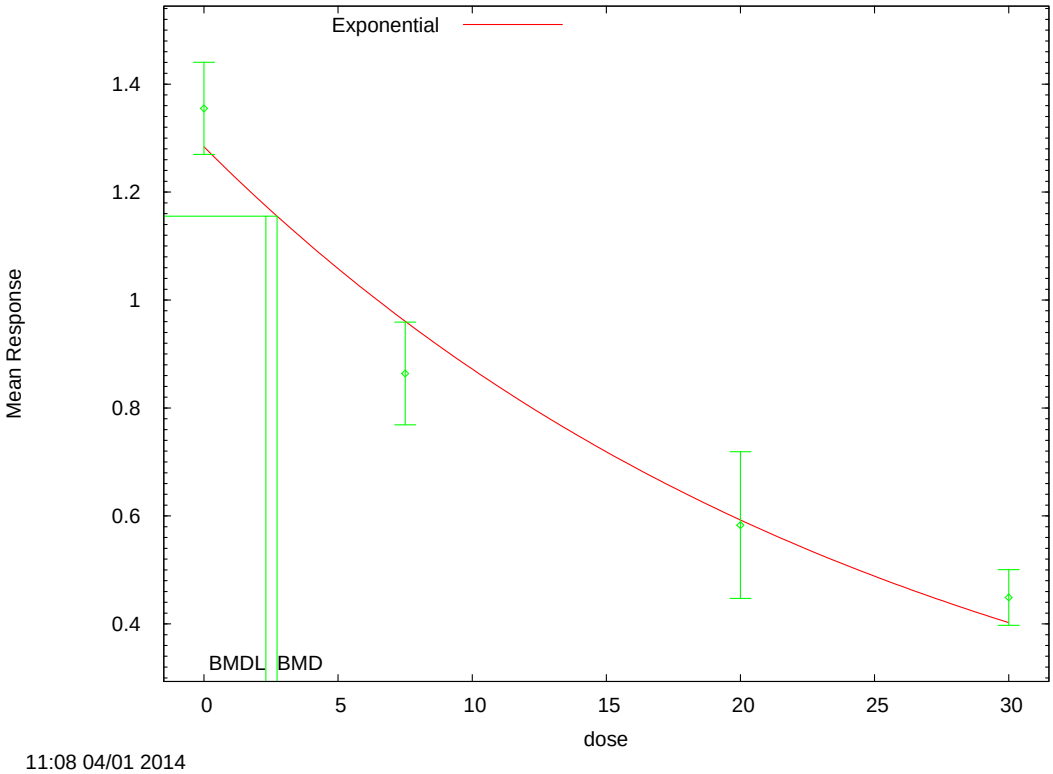
Risk Type = Relative deviation

Confidence Level = 0.950000

BMD and BMDL by Model

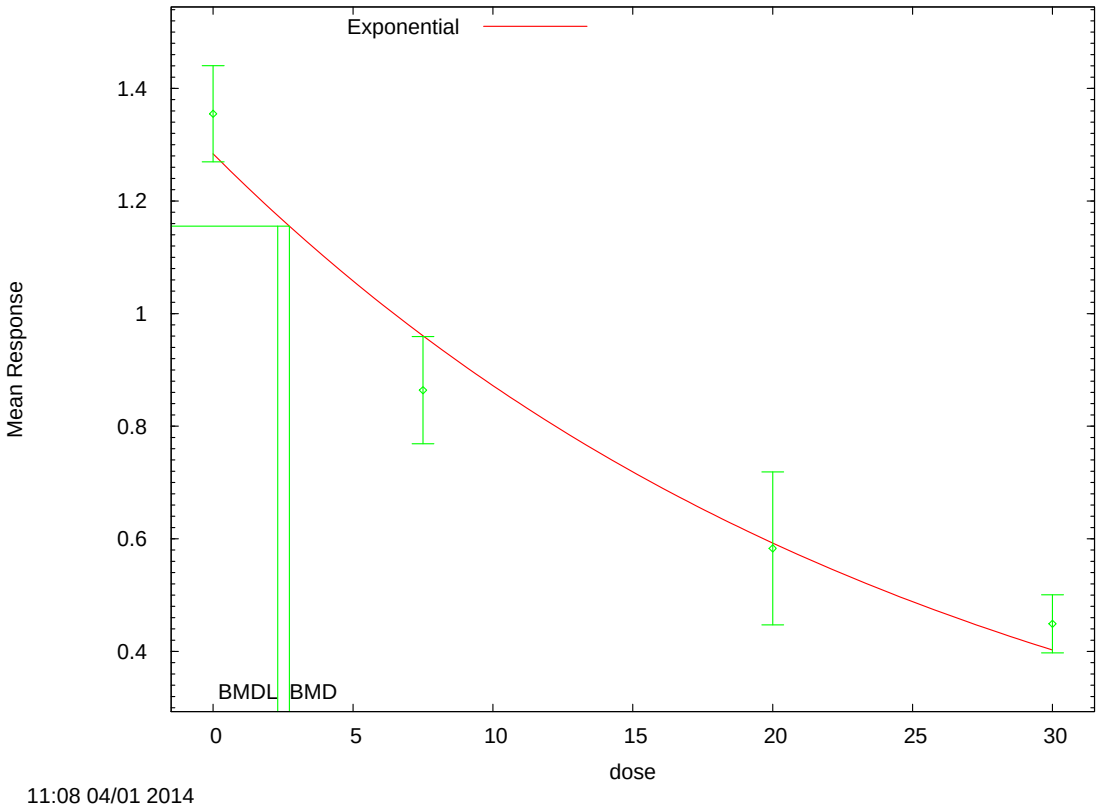
Model	BMD	BMDL
2	2.72511	2.31017
3	2.72511	2.31017
4	1.63675	1.27582
5	1.63675	1.27582

Exponential Model 2, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



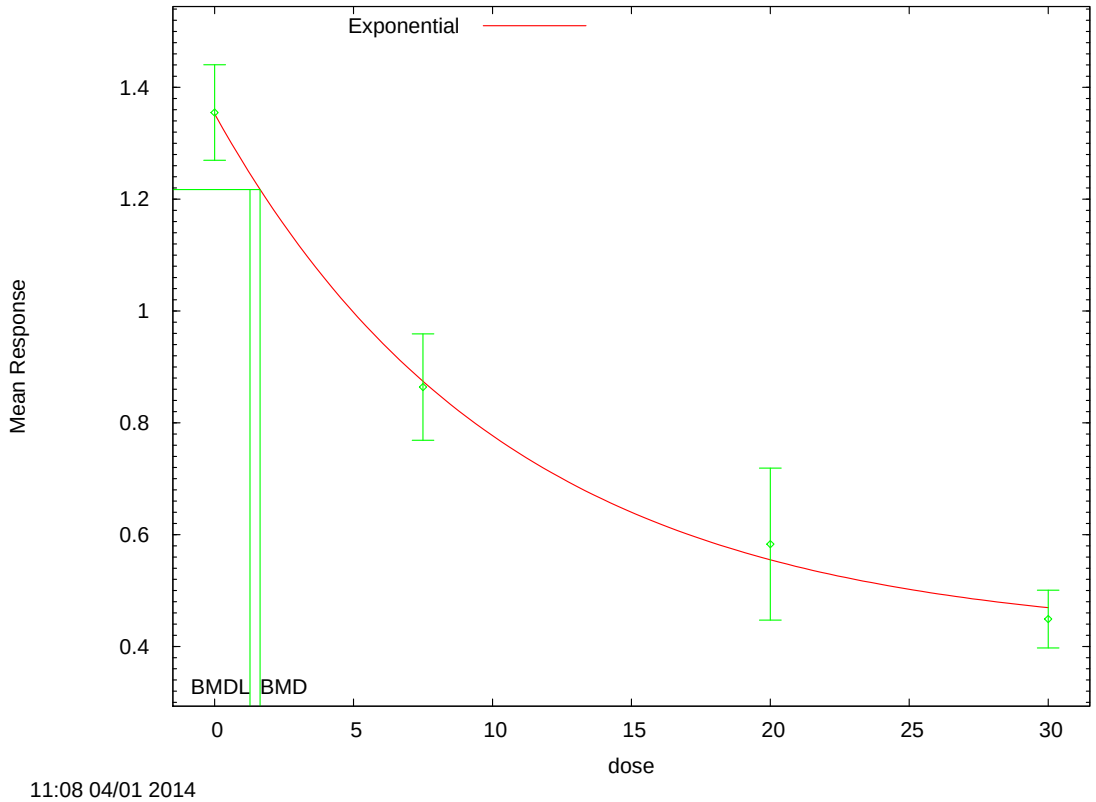
11:08 04/01 2014

Exponential Model 3, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



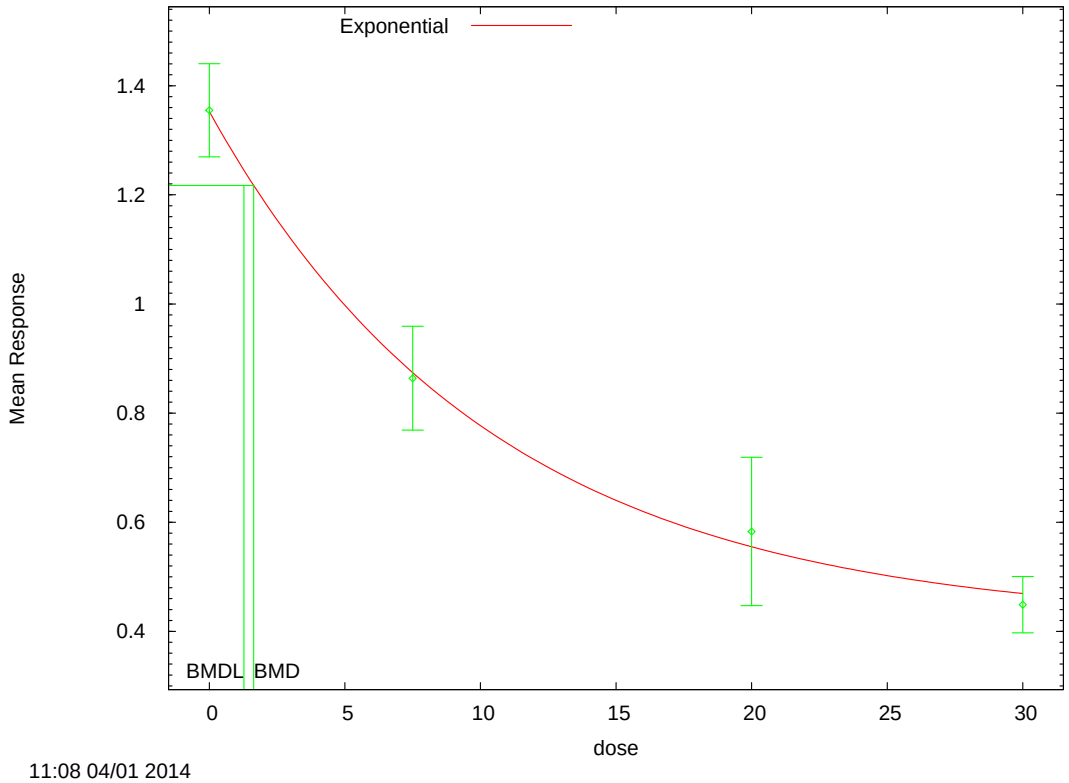
11:08 04/01 2014

Exponential Model 4, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



11:08 04/01 2014

Exponential Model 5, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



11:08 04/01 2014

MRID 49037406 - Repeat CCA Male Adult Brain ChE

```
 ================================================================
        Exponential Model. (Version: 1.9;  Date: 01/29/2013)
        Input Data File: F:/Pirimiphos-methyl/BMD runs/exp_Repeat CCA Adult Male
Brain_Setting.(d)
        Gnuplot Plotting File:
                                                Tue Apr 01 13:06:27 2014
 ================================================================

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                              Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha          -1.23004          -1.23004           -1.23004          -1.23004
         rho(S)              0                 0                  0                 0
           a           10.8155           10.8155            14.1383           14.1383
           b        0.00821588        0.00821588          0.0115401         0.0115401
           c                --                --             0.150938
0.150938
           d                --                 1                  --                 1

     (S) = Specified


                             Parameter Estimates by Model

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
```

lnalpha	-1.10119	-1.17248	-1.10119	-1.23004
rho	0	0	0	0
a	13.6798	13.5395	13.6798	13.465
b	0.00811135	0.0117129	0.00811135	0.0499066
c	--	--	0	0.776888
d	--	1.34285	--	2.42819

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	13.47	0.465
7.5	10	13.2	0.669
20	10	11.57	0.346
30	10	10.67	0.718

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	13.68	0.5766	-1.178
	7.5	12.87	0.5766	1.802
	20	11.63	0.5766	-0.3304
	30	10.73	0.5766	-0.3019
3	0	13.54	0.5564	-0.4237
	7.5	13.03	0.5564	0.9569
	20	11.74	0.5564	-0.9728
	30	10.59	0.5564	0.4427
4	0	13.68	0.5766	-1.178
	7.5	12.87	0.5766	1.802
	20	11.63	0.5766	-0.3304
	30	10.73	0.5766	-0.3019
5	0	13.46	0.5406	4.095e-008
	7.5	13.2	0.5406	5.662e-007
	20	11.57	0.5406	-1.585e-007
	30	10.67	0.5406	3.475e-007

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	4.600802	5	0.798395
A2	7.710123	8	0.5797533
A3	4.600802	5	0.798395

R	-29.72562	2	63.45124
2	2.023844	3	1.952312
3	3.449631	4	1.100739
4	2.023844	3	1.952312
5	4.600802	5	0.798395

Additive constant for all log-likelihoods = -36.76. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	74.87	6	< 0.0001
Test 2	6.219	3	0.1014
Test 3	6.219	3	0.1014
Test 4	5.154	2	0.076
Test 5a	2.302	1	0.1292
Test 5b	2.852	1	0.09128
Test 6a	5.154	2	0.076
Test 6b	4.21e-013	0	N/A
Test 7a	5.187e-013	0	N/A
Test 7b	2.302	1	0.1292
Test 7c	5.154	2	0.076

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is greater than .1. A homogeneous variance model appears to be appropriate here.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is less than .1. Model 2 may not adequately describe the data; you may want to consider another model.

The p-value for Test 5a is greater than .1. Model 3 seems to adequately describe the data.

The p-value for Test 5b is greater than .05. Model 3 does
not seem to fit the data better than Model 2.

The p-value for Test 6a is less than .1. Model 4 may not adequately
describe the data; you may want to consider another model.

Degrees of freedom for Test 6b are less than or equal to 0.
The Chi-Square test for fit is not valid.

Degrees of freedom for Test 7a are less than or equal to 0.
The Chi-Square test for fit is not valid.

The p-value for Test 7b is greater than .05. Model 5 does
not seem to fit the data better than Model 3.

The p-value for Test 7c is greater than .05. Model 5 does
not seem to fit the data better than Model 4.

Benchmark Dose Computations:

Specified Effect = 0.100000

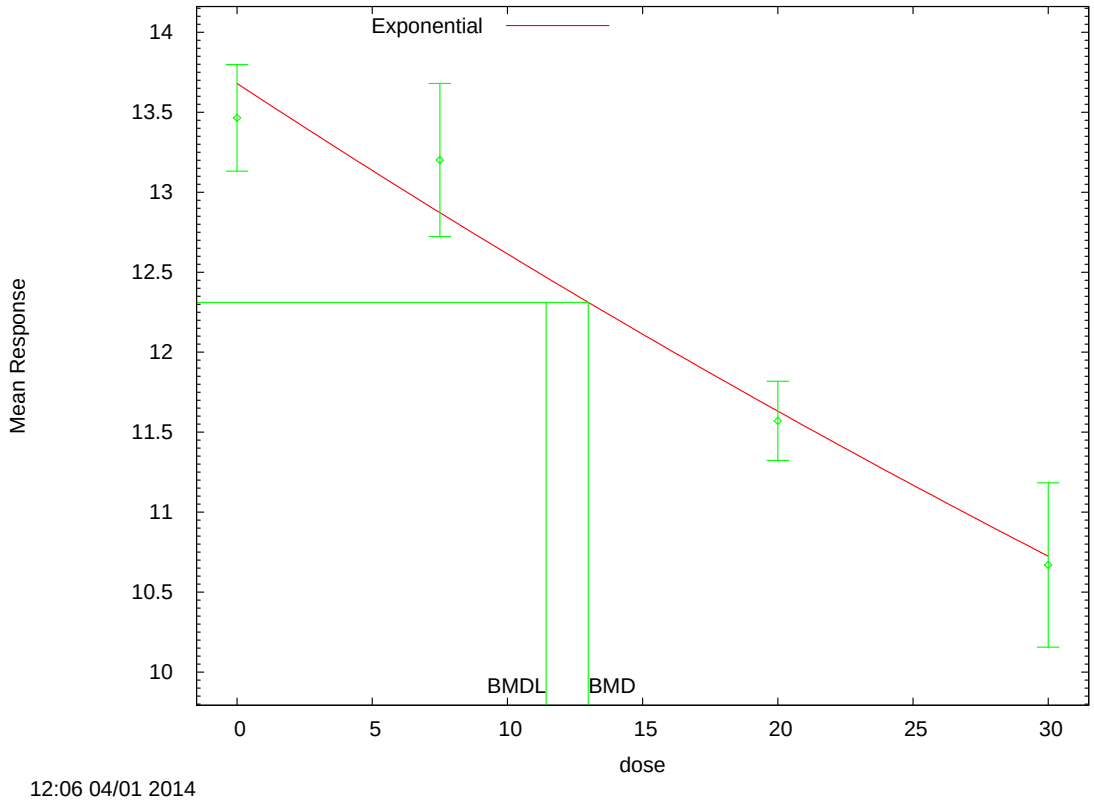
Risk Type = Relative deviation

Confidence Level = 0.950000

BMD and BMDL by Model

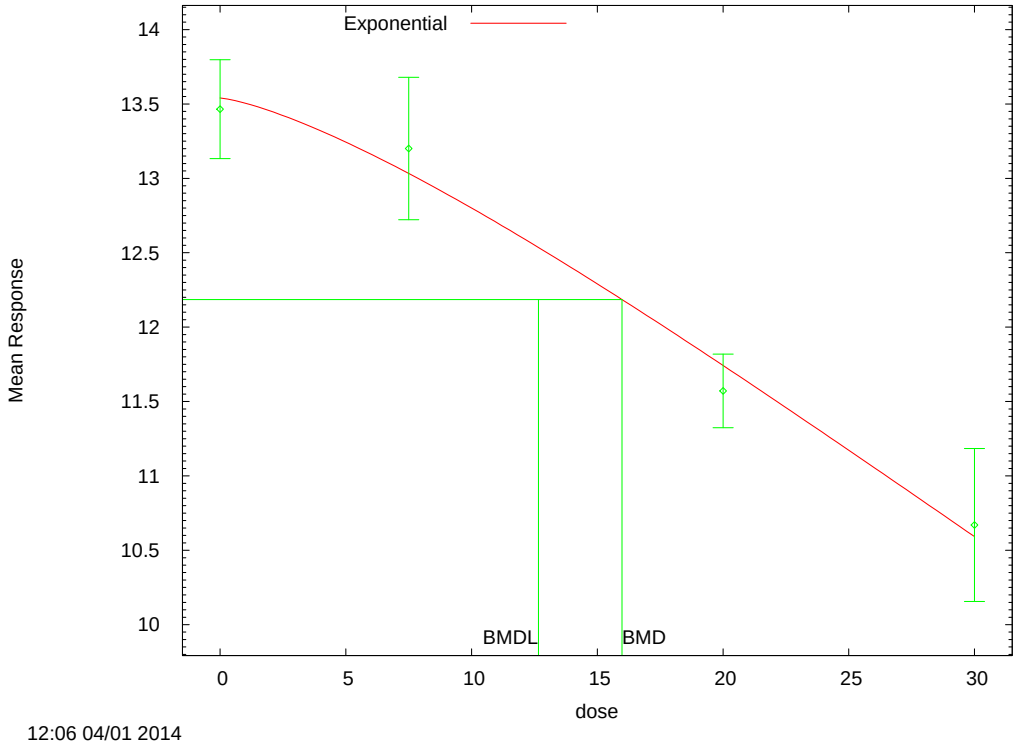
Model	BMD	BMDL
2	12.9893	11.4333
3	15.9785	12.6578
4	12.9893	11.0254
5	16.1754	13.0084

Exponential Model 2, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



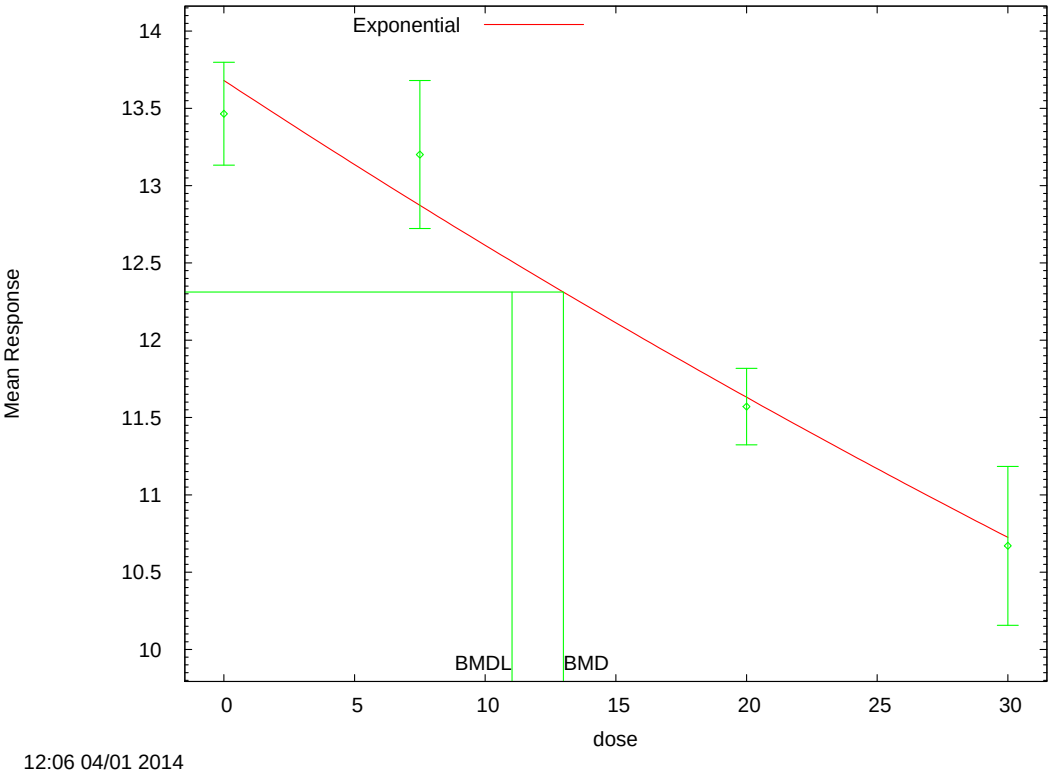
12:06 04/01 2014

Exponential Model 3, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



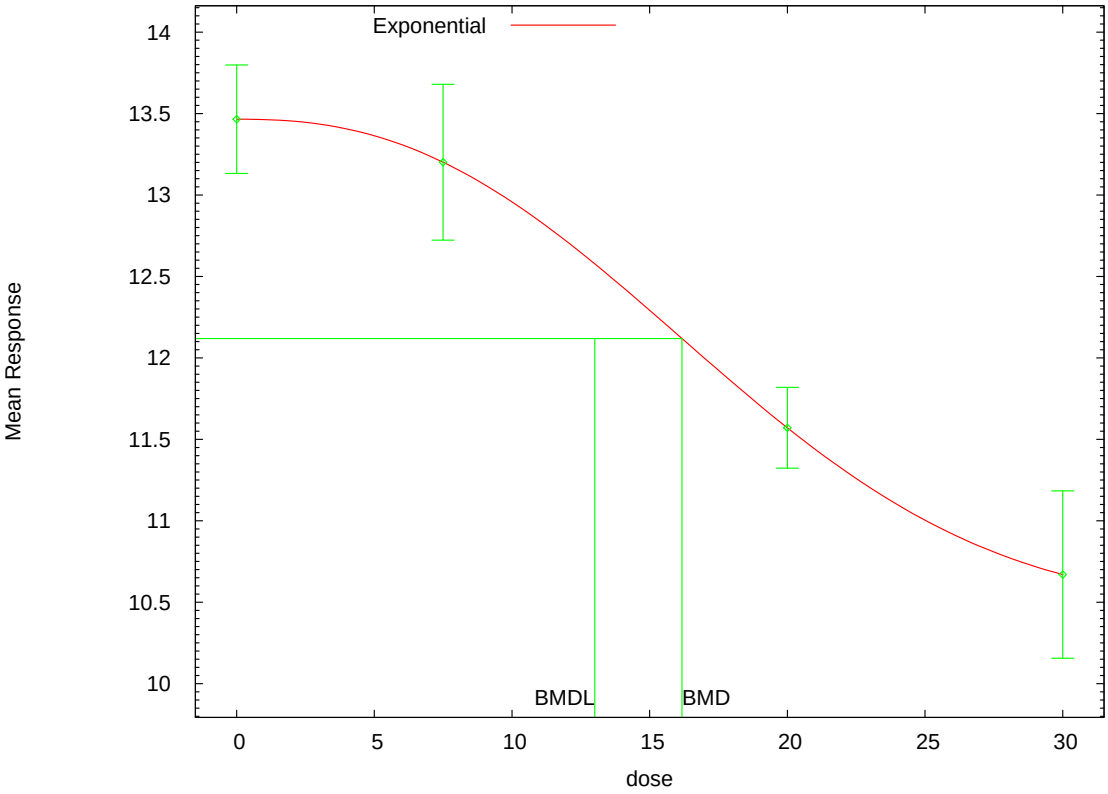
12:06 04/01 2014

Exponential Model 4, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



12:06 04/01 2014

Exponential Model 5, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



12:06 04/01 2014

MRID 49037406 - Repeat CCA Female Adult Brain ChE

```
 ================================================================
        Exponential Model. (Version: 1.9;  Date: 01/29/2013)
        Input Data File: F:/Pirimiphos-methyl/BMD runs/exp_Repeat CCA Adult Female
Brain_Setting.(d)
        Gnuplot Plotting File:
                                                Tue Apr 01 13:21:28 2014
 ================================================================

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha         -0.497991         -0.497991         -0.497991         -0.497991
         rho(S)              0                 0                 0                 0
           a            10.017            10.017            14.8166           14.8166
           b         0.0109456         0.0109456         0.0801879         0.0801879
           c                --                --               0.653002
0.653002
           d                --                 1                --                 1

     (S) = Specified
```

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	-0.337136	-0.337136	-0.495137	-0.497991
rho	0	0	0	0
a	13.8051	13.8051	14.1247	14.111
b	0.0113867	0.0113867	0.0657675	0.0778887
c	--	--	0.671121	0.699638
d	--	1	--	1.16789

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	14.11	0.868
7.5	10	12.36	0.632
20	10	10.66	0.768
30	10	10.16	0.979

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	13.81	0.8449	1.145
	7.5	12.68	0.8449	-1.187
	20	10.99	0.8449	-1.233
	30	9.81	0.8449	1.305
3	0	13.81	0.8449	1.145
	7.5	12.68	0.8449	-1.187
	20	10.99	0.8449	-1.233
	30	9.81	0.8449	1.305
4	0	14.12	0.7807	-0.05547
	7.5	12.32	0.7807	0.1702
	20	10.73	0.7807	-0.2515
	30	10.13	0.7807	0.1367
5	0	14.11	0.7796	-4.673e-007
	7.5	12.36	0.7796	1.884e-007
	20	10.66	0.7796	4.01e-007
	30	10.16	0.7796	-6.233e-007

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC

A1	-10.04018	5	30.08036
A2	-9.036603	8	34.07321
A3	-10.04018	5	30.08036
R	-42.07921	2	88.15841
2	-13.25729	3	32.51458
3	-13.25729	3	32.51458
4	-10.09727	4	28.19453
5	-10.04018	5	30.08036

Additive constant for all log-likelihoods = -36.76. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	66.09	6	< 0.0001
Test 2	2.007	3	0.5709
Test 3	2.007	3	0.5709
Test 4	6.434	2	0.04007
Test 5a	6.434	2	0.04007
Test 5b	-5.507e-013	0	N/A
Test 6a	0.1142	1	0.7354
Test 6b	6.32	1	0.01194
Test 7a	8.562e-013	0	N/A
Test 7b	6.434	2	0.04007
Test 7c	0.1142	1	0.7354

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is greater than .1. A homogeneous variance model appears to be appropriate here.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is less than .1. Model 2 may not adequately describe the data; you may want to consider another model.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Degrees of freedom for Test 5b are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

The p-value for Test 6b is less than .05. Model 4 appears to fit the data better than Model 2.

Degrees of freedom for Test 7a are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 7b is less than .05. Model 5 appears to fit the data better than Model 3.

The p-value for Test 7c is greater than .05. Model 5 does not seem to fit the data better than Model 4.

Benchmark Dose Computations:

Specified Effect = 0.100000

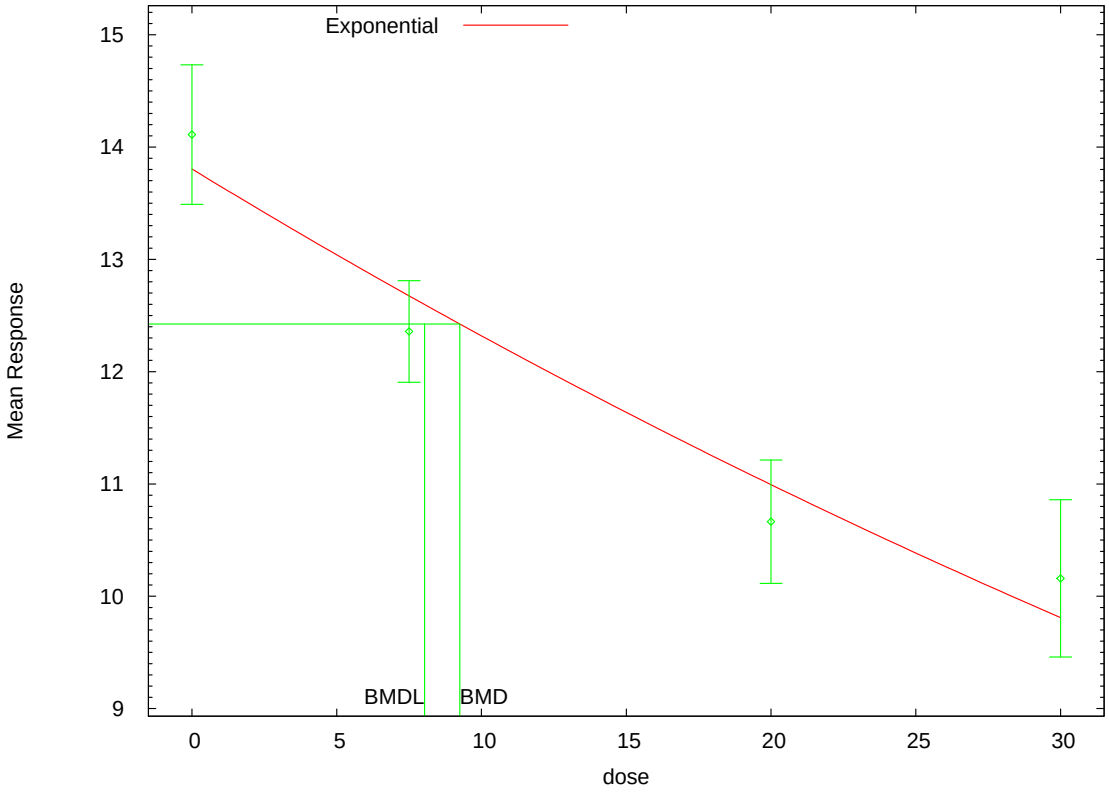
Risk Type = Relative deviation

Confidence Level = 0.950000

BMD and BMDL by Model

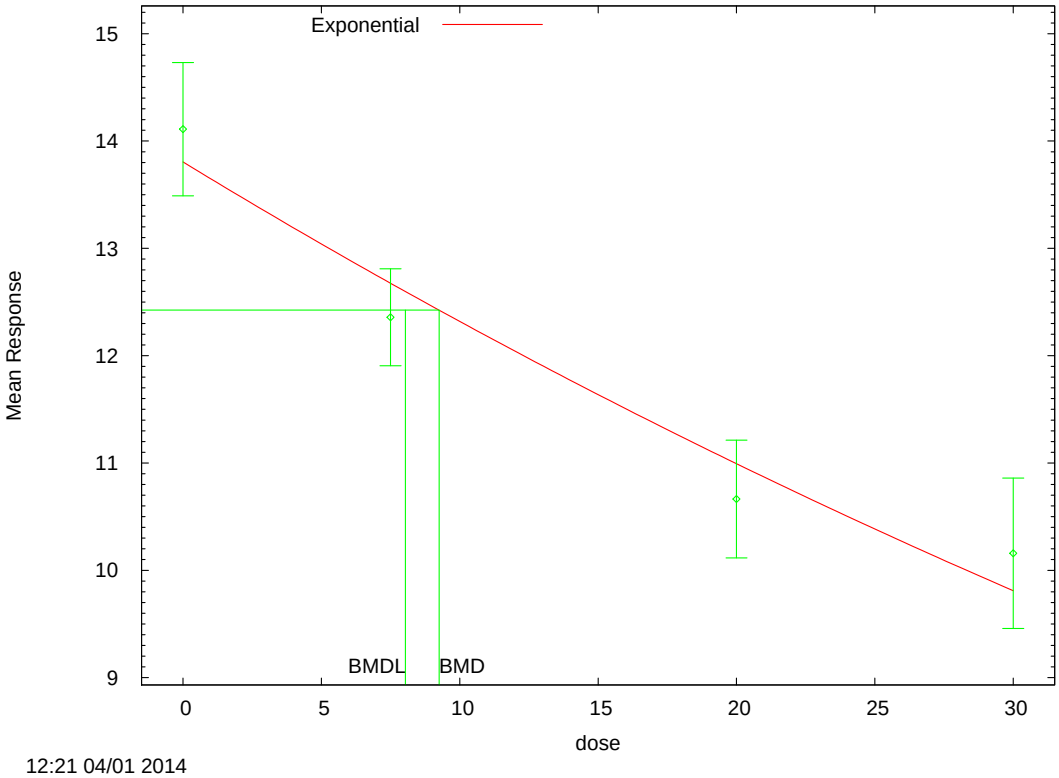
Model	BMD	BMDL
2	9.25295	8.03716
3	9.25295	8.03716
4	5.51179	3.92254
5	5.91951	3.95143

Exponential Model 2, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



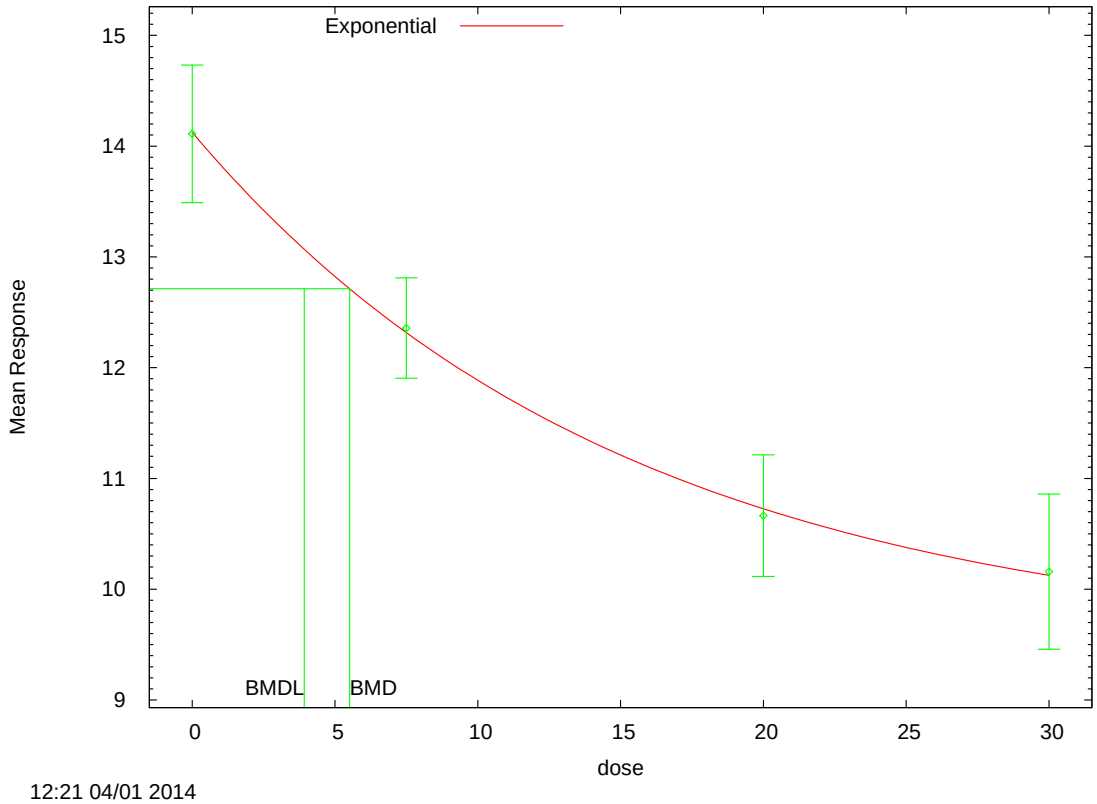
12:21 04/01 2014

Exponential Model 3, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



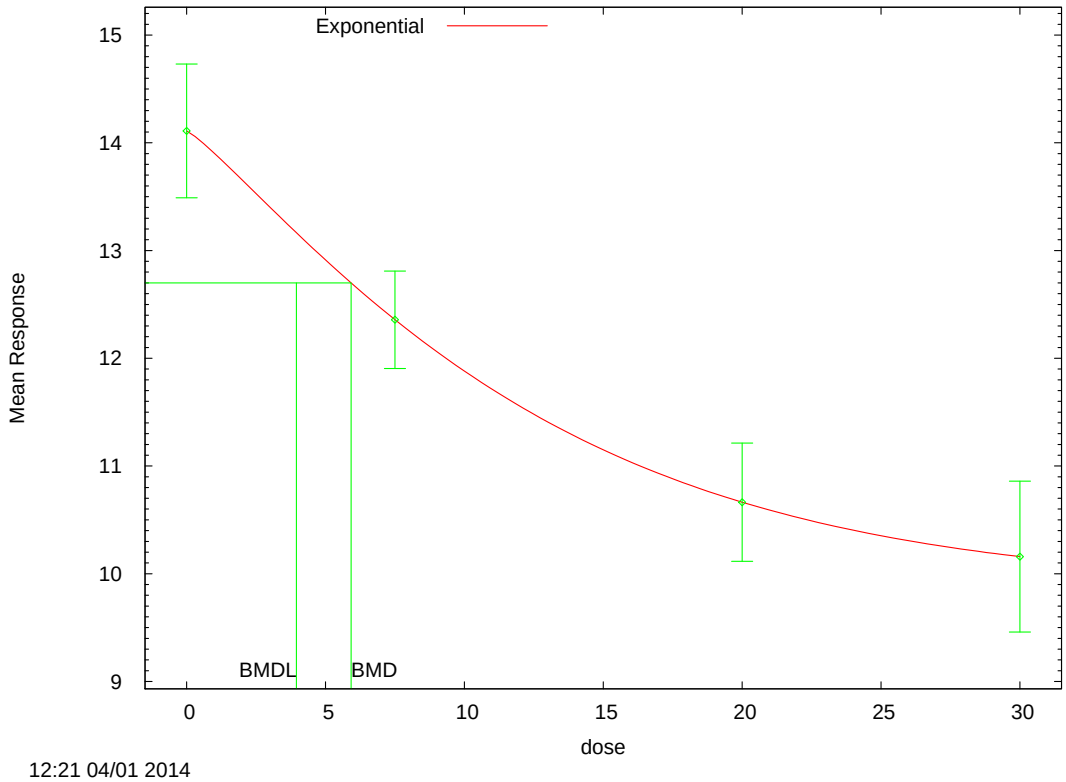
12:21 04/01 2014

Exponential Model 4, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



12:21 04/01 2014

Exponential Model 5, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



12:21 04/01 2014

MRID 49037406 - Repeat CCA Male Pup PND21 RBC ChE – Non-Constant Variance

```
 ================================================================
        Exponential Model. (Version: 1.9;  Date: 01/29/2013)
        Input Data File: F:/Pirimiphos-methyl/BMD runs/exp_Repeat CCA Male Pup PND21
RBC_Setting.(d)
        Gnuplot Plotting File:
                                                Tue Apr 01 14:32:45 2014
 ================================================================

 BMDS Model Run
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   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log(mean(i)) * rho)

   Total number of dose groups = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                              Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha          -3.08665          -3.08665           -3.08665          -3.08665
         rho           3.02145           3.02145            3.02145           3.02145
           a          0.837283           1.03968             2.4108            2.4108
           b         0.0534454        0.00150616           0.192996          0.192996
           c                --                --               0.295496
0.295496
           d                --                 2                    --                 1


                              Parameter Estimates by Model

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha       -2.89576          -2.89576          -3.04973          -3.16489
         rho           3.22417           3.22416             2.91929           2.99464
           a           1.96988           1.96988             2.39066           2.26215
```

b	0.0498742	0.0498742	0.179192	0.169411
c	--	--	0.290936	0.333051
d	--	1	--	1.95238

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	9	2.296	0.699
3.75	8	1.693	0.578
7.5	9	1.083	0.192
20	10	0.748	0.152

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	1.97	0.7012	1.395
	3.75	1.634	0.5187	0.3225
	7.5	1.355	0.3837	-2.128
	20	0.7265	0.1404	0.484
3	0	1.97	0.7012	1.395
	3.75	1.634	0.5187	0.3225
	7.5	1.355	0.3837	-2.128
	20	0.7265	0.1404	0.484
4	0	2.391	0.7767	-0.3656
	3.75	1.561	0.417	0.8937
	7.5	1.138	0.2627	-0.624
	20	0.7426	0.141	0.1211
5	0	2.262	0.6976	0.1456
	3.75	1.752	0.4759	-0.3523
	7.5	1.059	0.224	0.3186
	20	0.7534	0.1345	-0.128

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	12.13093	5	-14.26185
A2	25.42045	8	-34.84091
A3	24.71212	6	-37.42424
R	-7.22808	2	18.45616
2	18.69677	4	-29.39354
3	18.69677	4	-29.39354

4	22.89332	5	-35.78664
5	24.71212	6	-37.42424

Additive constant for all log-likelihoods = -33.08. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	65.3	6	< 0.0001
Test 2	26.58	3	< 0.0001
Test 3	1.417	2	0.4925
Test 4	12.03	2	0.002441
Test 5a	12.03	2	0.002441
Test 5b	-1.727e-011	0	N/A
Test 6a	3.638	1	0.05649
Test 6b	8.393	1	0.003766
Test 7a	-1.258e-012	0	N/A
Test 7b	12.03	2	0.002441
Test 7c	3.638	1	0.05649

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is less than .1. Model 2 may not adequately describe the data; you may want to consider another model.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Degrees of freedom for Test 5b are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 6a is less than .1. Model 4 may not adequately describe the data; you may want to consider another model.

The p-value for Test 6b is less than .05. Model 4 appears to fit the data better than Model 2.

Degrees of freedom for Test 7a are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 7b is less than .05. Model 5 appears to fit the data better than Model 3.

The p-value for Test 7c is greater than .05. Model 5 does not seem to fit the data better than Model 4.

Benchmark Dose Computations:

Specified Effect = 0.100000

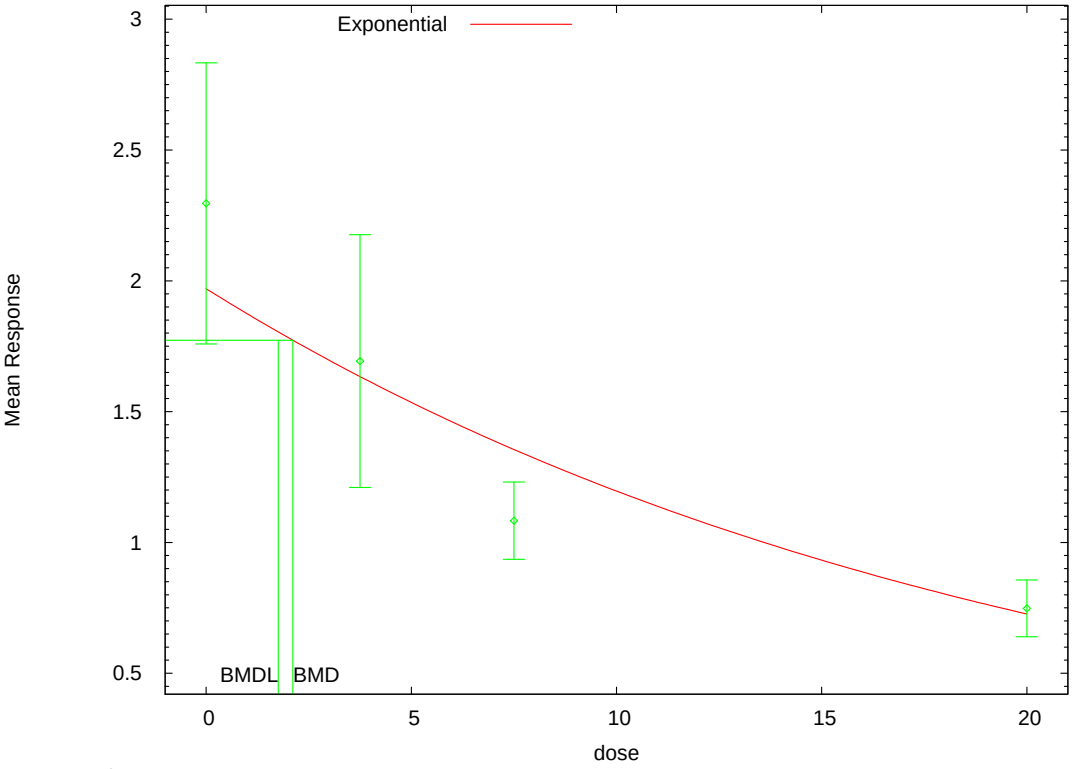
Risk Type = Relative deviation

Confidence Level = 0.950000

BMD and BMDL by Model

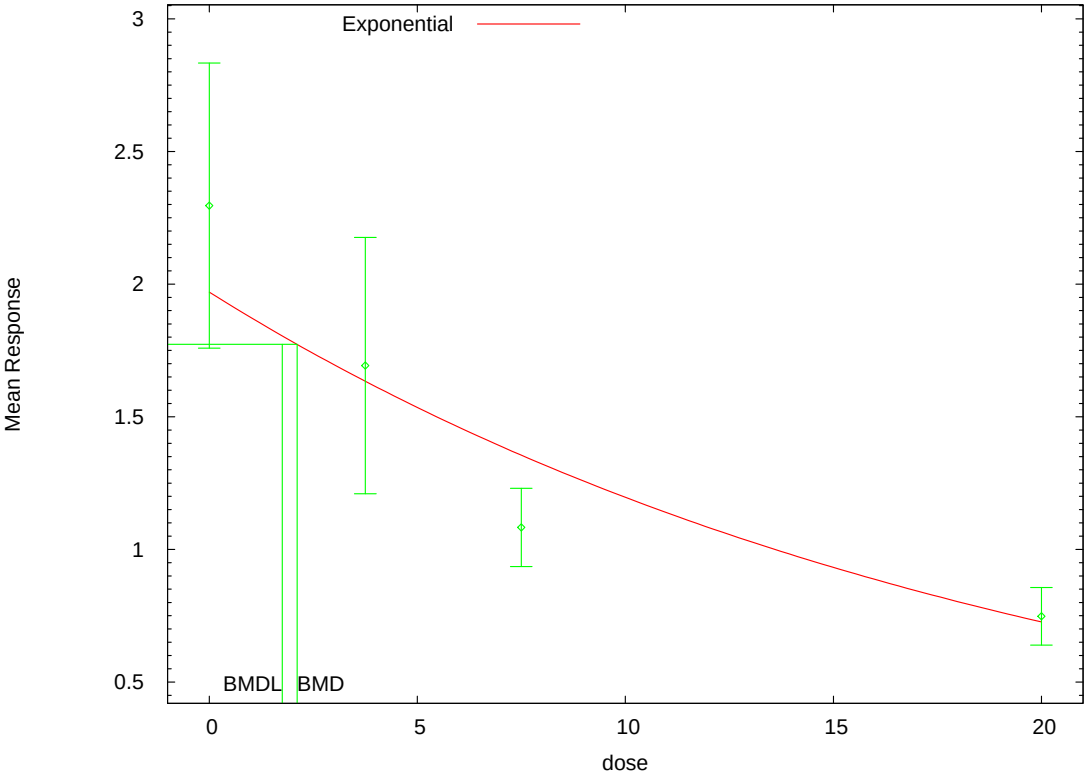
Model	BMD	BMDL
2	2.11253	1.75626
3	2.11253	1.75626
4	0.848375	0.600399
5	2.32693	0.984078

Exponential Model 2, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



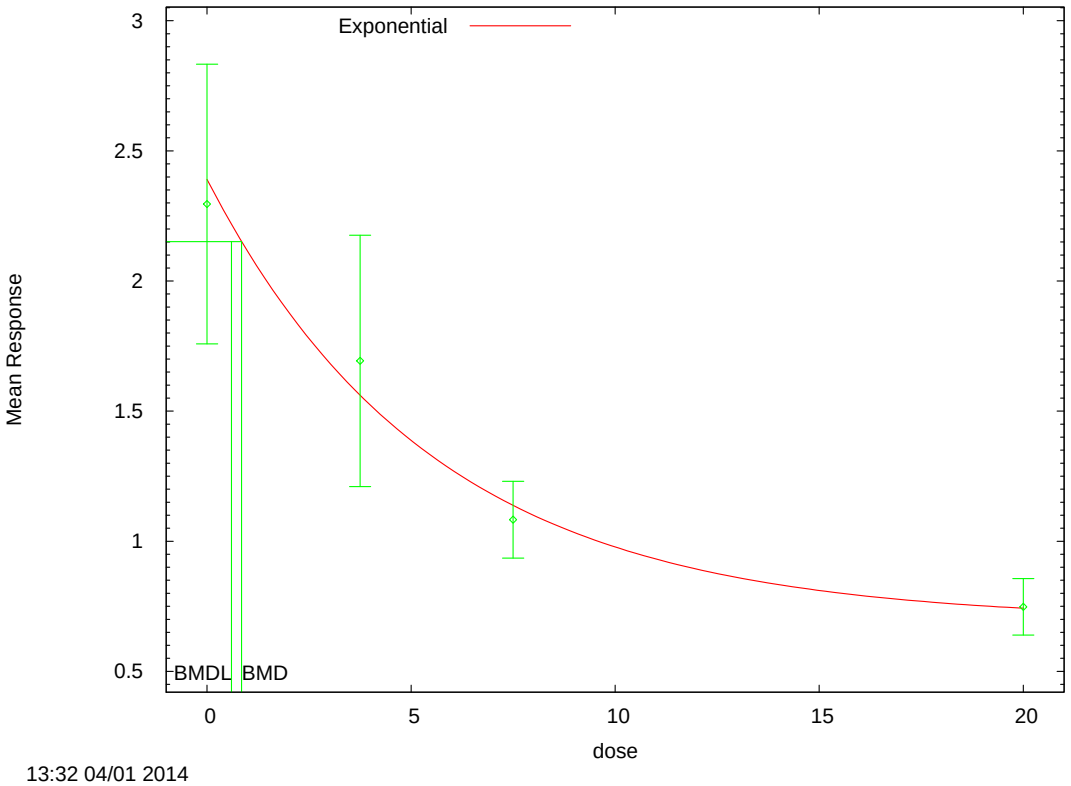
13:32 04/01 2014

Exponential Model 3, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



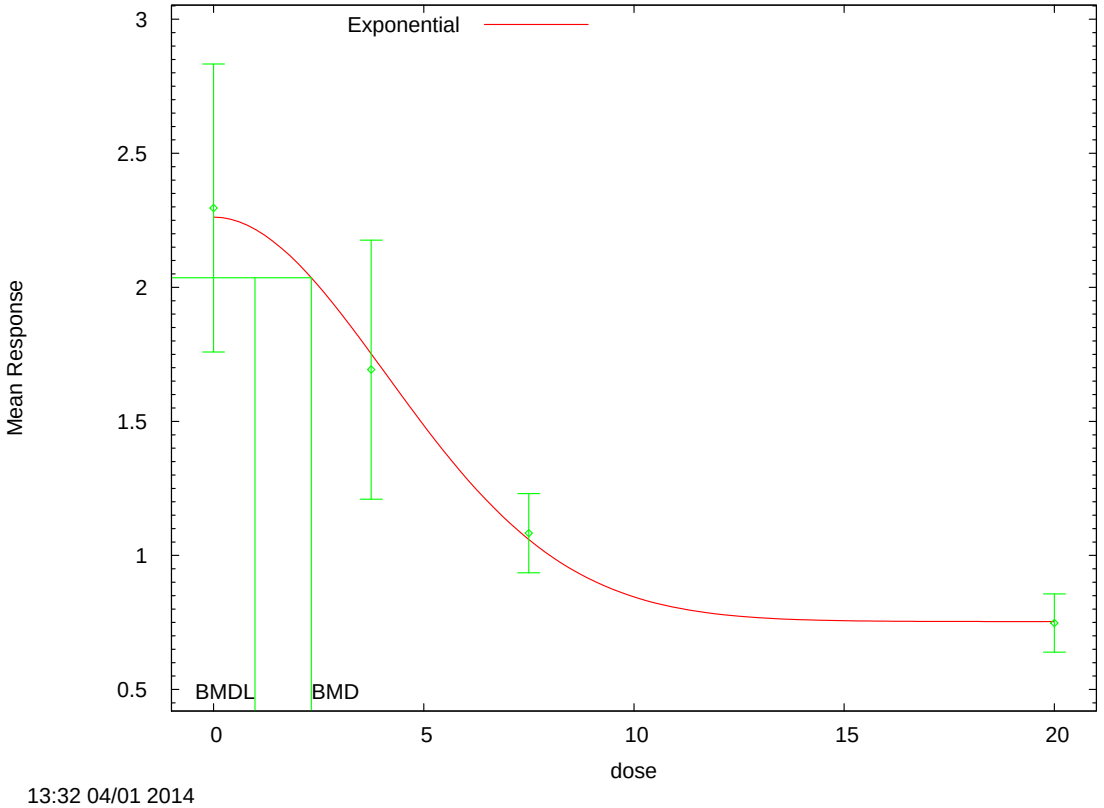
13:32 04/01 2014

Exponential Model 4, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



13:32 04/01 2014

Exponential Model 5, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



13:32 04/01 2014

MRID 49037406 - Repeat CCA Female Pup PND21 RBC ChE – Non-Constant Variance

```
 ======================================================================
        Exponential Model. (Version: 1.9;  Date: 01/29/2013)
        Input Data File: F:/Pirimiphos-methyl/BMD runs/exp_Repeat CCA Female Pup
PND21 RBC_Setting.(d)
        Gnuplot Plotting File:
                                                Tue Apr 01 16:01:58 2014
 ======================================================================

 BMDS Model Run
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   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log(mean(i)) * rho)

   Total number of dose groups = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha          -2.37996          -2.37996           -2.37996          -2.37996
         rho           1.03043           1.03043            1.03043           1.03043
           a          0.843328            1.0548            2.64285           2.64285
           b         0.0620132        0.00182755           0.200057          0.200057
           c                --                --               0.245046
0.245046
           d                --                 2                  --                 1


                               Parameter Estimates by Model

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha        -2.2162           -2.2162           -2.23279          -2.23279
```

rho	1.21187	1.21187	0.978566	0.978566
a	2.29332	2.29332	2.48029	2.48029
b	0.0661554	0.0661554	0.135598	0.135598
c	--	--	0.216535	0.216535
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	2.517	0.522
3.75	10	1.655	0.257
7.5	10	1.24	0.557
20	10	0.68	0.219

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	2.293	0.546	1.296
	3.75	1.789	0.4698	-0.9052
	7.5	1.396	0.4042	-1.223
	20	0.6107	0.2449	0.8945
3	0	2.293	0.546	1.296
	3.75	1.789	0.4698	-0.9052
	7.5	1.396	0.4042	-1.223
	20	0.6107	0.2449	0.8945
4	0	2.48	0.5107	0.2273
	3.75	1.706	0.4252	-0.3772
	7.5	1.24	0.3638	0.000881
	20	0.6661	0.2684	0.1636
5	0	2.48	0.5107	0.2273
	3.75	1.706	0.4252	-0.3772
	7.5	1.24	0.3638	0.0008807
	20	0.6661	0.2684	0.1636

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	17.05987	5	-24.11974
A2	23.23362	8	-30.46723
A3	18.90464	6	-25.80928
R	-9.976443	2	23.95289

2	16.73367	4	-25.46733
3	16.73367	4	-25.46733
4	18.53445	5	-27.06889
5	18.53445	5	-27.06889

Additive constant for all log-likelihoods = -36.76. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	66.42	6	< 0.0001
Test 2	12.35	3	0.006283
Test 3	8.658	2	0.01318
Test 4	4.342	2	0.1141
Test 5a	4.342	2	0.1141
Test 5b	-3.1e-011	0	N/A
Test 6a	0.7404	1	0.3895
Test 6b	3.602	1	0.05773
Test 7a	0.7404	1	0.3895
Test 7b	3.602	1	0.05773
Test 7c	-2.359e-012	0	N/A

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 4 is greater than .1. Model 2 seems to adequately describe the data.

The p-value for Test 5a is greater than .1. Model 3 seems to adequately describe the data.

Degrees of freedom for Test 5b are less than or equal to 0.

The Chi-Square test for fit is not valid.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

The p-value for Test 6b is greater than .05. Model 4 does not seem to fit the data better than Model 2.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

The p-value for Test 7b is greater than .05. Model 5 does not seem to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0. The Chi-Square test for fit is not valid.

Benchmark Dose Computations:

Specified Effect = 0.100000

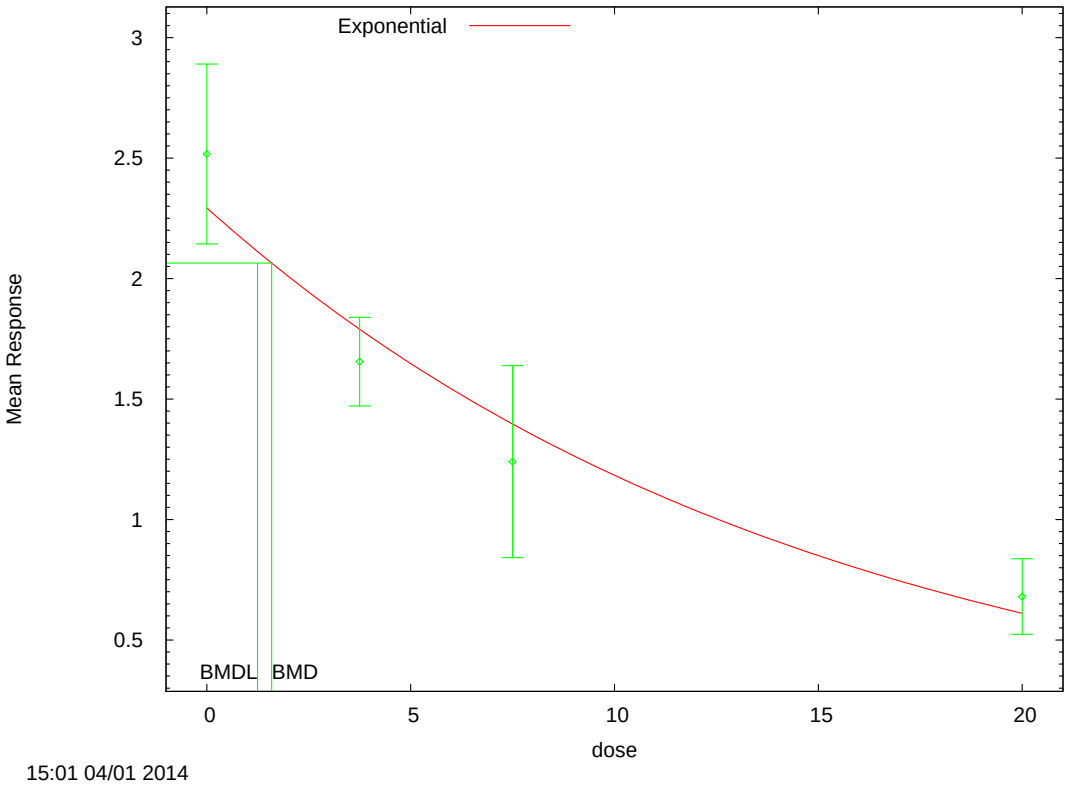
Risk Type = Relative deviation

Confidence Level = 0.950000

BMD and BMDL by Model

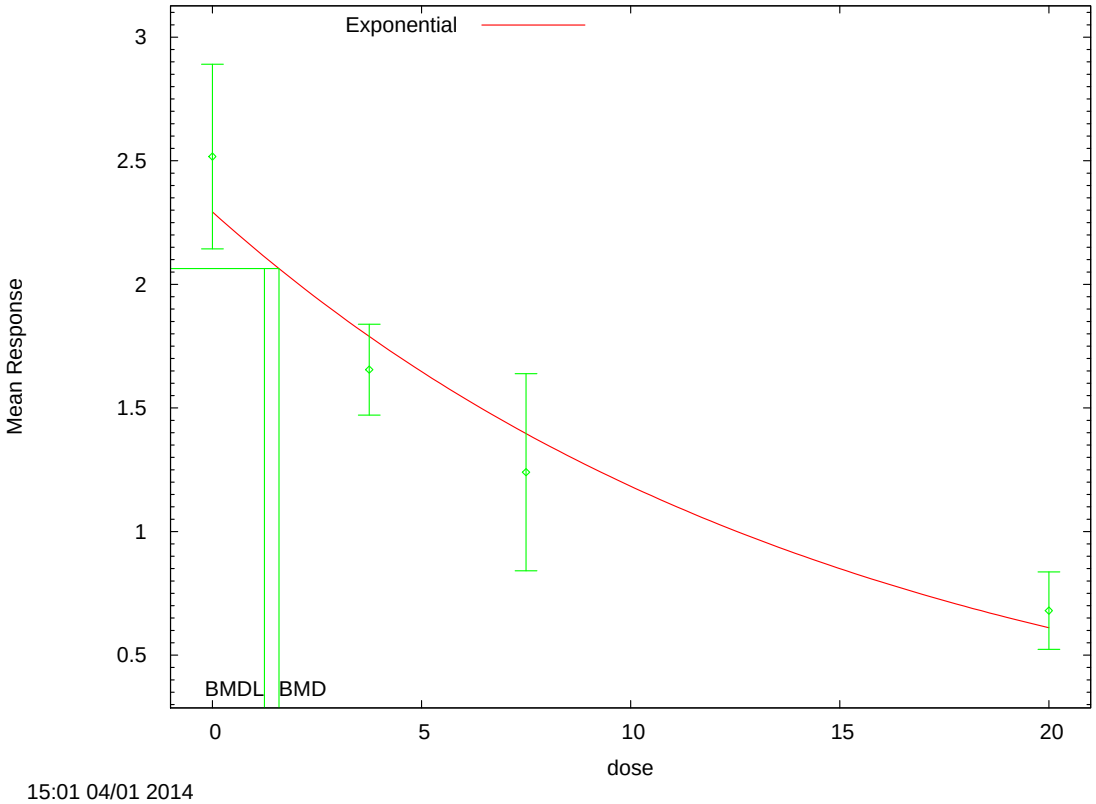
Model	BMD	BMDL
2	1.59262	1.24504
3	1.59262	1.24504
4	1.00703	0.7275
5	1.00703	0.7275

Exponential Model 2, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



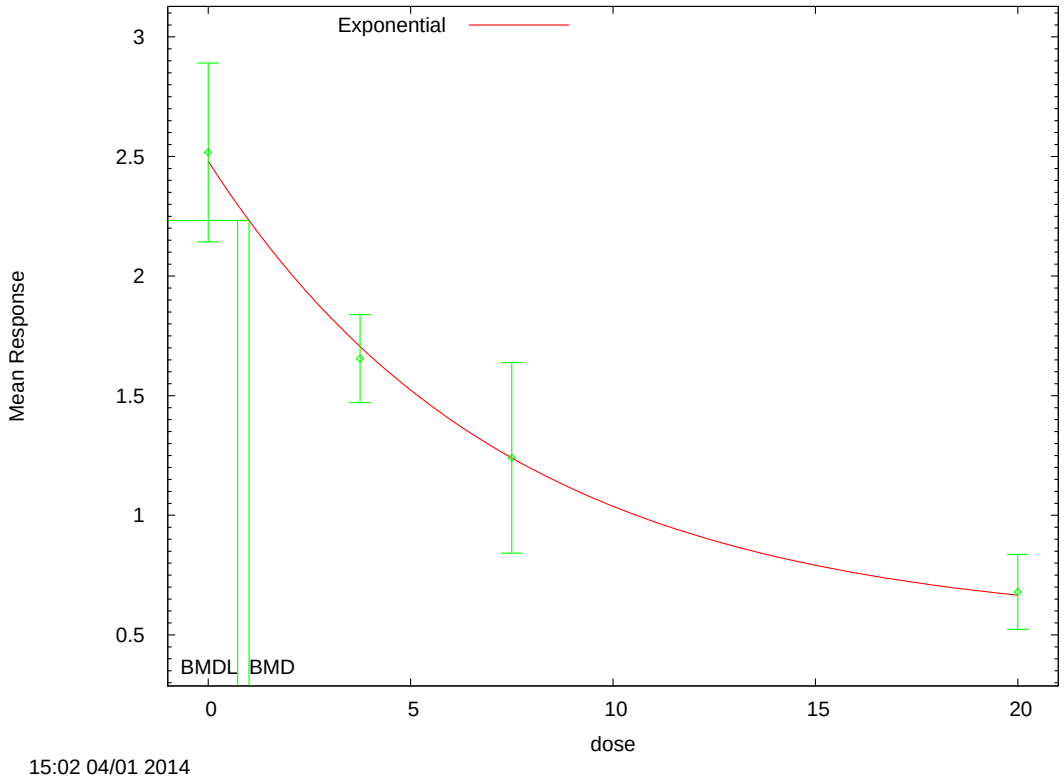
15:01 04/01 2014

Exponential Model 3, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



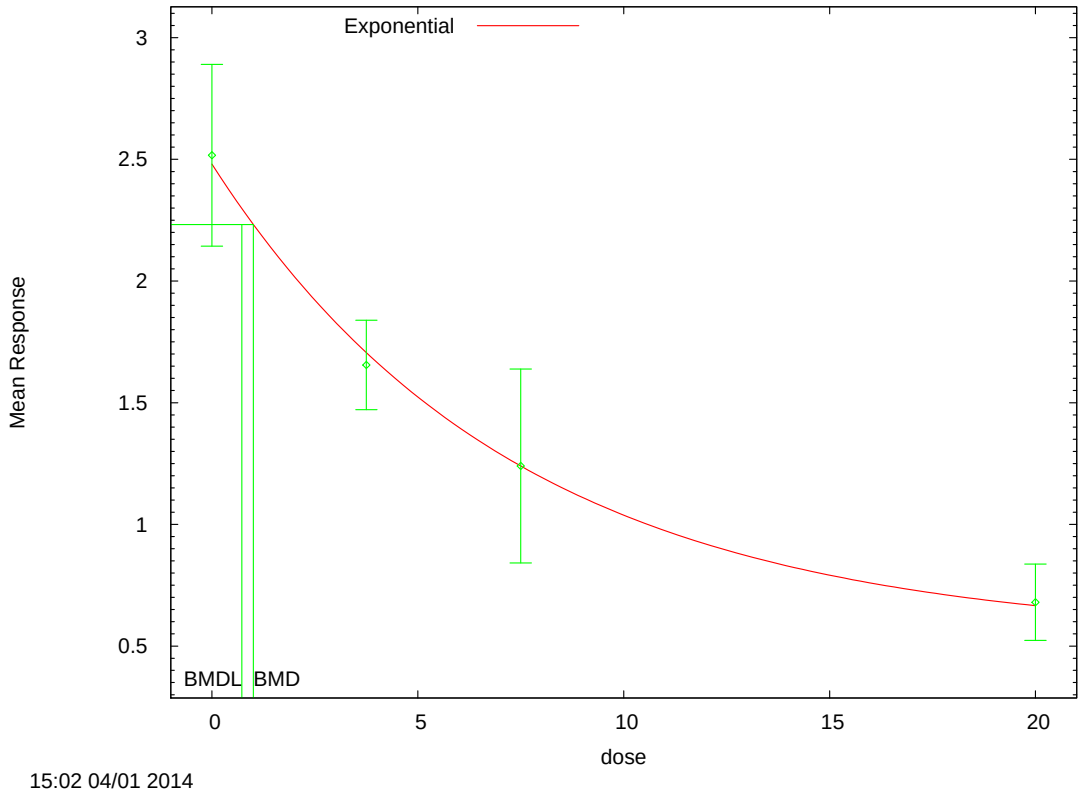
15:01 04/01 2014

Exponential Model 4, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



15:02 04/01 2014

Exponential Model 5, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



15:02 04/01 2014

MRID 49037406 Repeat CCA Male Pup PND21 Brain
CONSTANT VARIANCE - YES

```
 ================================================================
        Exponential Model. (Version: 1.7;  Date: 12/10/2009)
        Input Data File: C:/Users/EHolman/Desktop/HED Desktop/BMDS220/Data/exp_Repeat
CCA Male Pup PND21 Brain_Setting.(d)
        Gnuplot Plotting File:
                                              Sat Apr 05 11:53:09 2014
 ================================================================

 BMDS Model Run
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   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 250
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha          -1.45832          -1.45832           -1.45832          -1.45832
         rho(S)              0                 0                  0                 0
           a           7.42708           7.42708            10.8822           10.8822
           b         0.0192654         0.0192654           0.127685          0.127685
           c                --                --              0.616647
0.616647
           d                --                 1                 --                 1

     (S) = Specified
```

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	-0.91994	-0.91994	-1.13348	-1.45832
rho	0	0	0	0
a	10.208	10.208	10.4887	10.364
b	0.0202975	0.0202975	0.0916212	0.14252
c	--	--	0.602865	0.679853
d	--	1	--	2.59087

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	10.36	0.48
3.75	8	9.77	0.318
7.5	9	8.057	0.415
20	10	7.046	0.703

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	10.21	0.6313	0.7812
	3.75	9.46	0.6313	1.389
	7.5	8.767	0.6313	-3.372
	20	6.802	0.6313	1.222
3	0	10.21	0.6313	0.7812
	3.75	9.46	0.6313	1.389
	7.5	8.767	0.6313	-3.372
	20	6.802	0.6313	1.222
4	0	10.49	0.5674	-0.6952
	3.75	9.278	0.5674	2.455
	7.5	8.419	0.5674	-1.912
	20	6.99	0.5674	0.3129
5	0	10.36	0.4823	1.374e-008
	3.75	9.77	0.4823	-3.93e-008
	7.5	8.057	0.4823	1.995e-008
	20	7.046	0.4823	5.193e-008

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC

A1	8.479008	5	-6.958017
A2	11.56235	8	-7.124704
A3	8.479008	5	-6.958017
R	-31.892	2	67.78399
2	-1.481118	3	8.962236
3	-1.481118	3	8.962236
4	2.469408	4	3.061184
5	8.479008	5	-6.958017

Additive constant for all log-likelihoods = -34. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	86.91	6	< 0.0001
Test 2	6.167	3	0.1038
Test 3	6.167	3	0.1038
Test 4	19.92	2	< 0.0001
Test 5a	19.92	2	< 0.0001
Test 5b	-1.07e-013	0	N/A
Test 6a	12.02	1	0.0005266
Test 6b	7.901	1	0.004941
Test 7a	7.105e-015	0	N/A
Test 7b	19.92	2	< 0.0001
Test 7c	12.02	1	0.0005266

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is greater than .1. A homogeneous variance model appears to be appropriate here.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is less than .1. Model 2 may not adequately describe the data; you may want to consider another model.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Degrees of freedom for Test 5b are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 6a is less than .1. Model 4 may not adequately describe the data; you may want to consider another model.

The p-value for Test 6b is less than .05. Model 4 appears to fit the data better than Model 2.

Degrees of freedom for Test 7a are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 7b is less than .05. Model 5 appears to fit the data better than Model 3.

The p-value for Test 7c is less than .05. Model 5 appears to fit the data better than Model 4.

Benchmark Dose Computations:

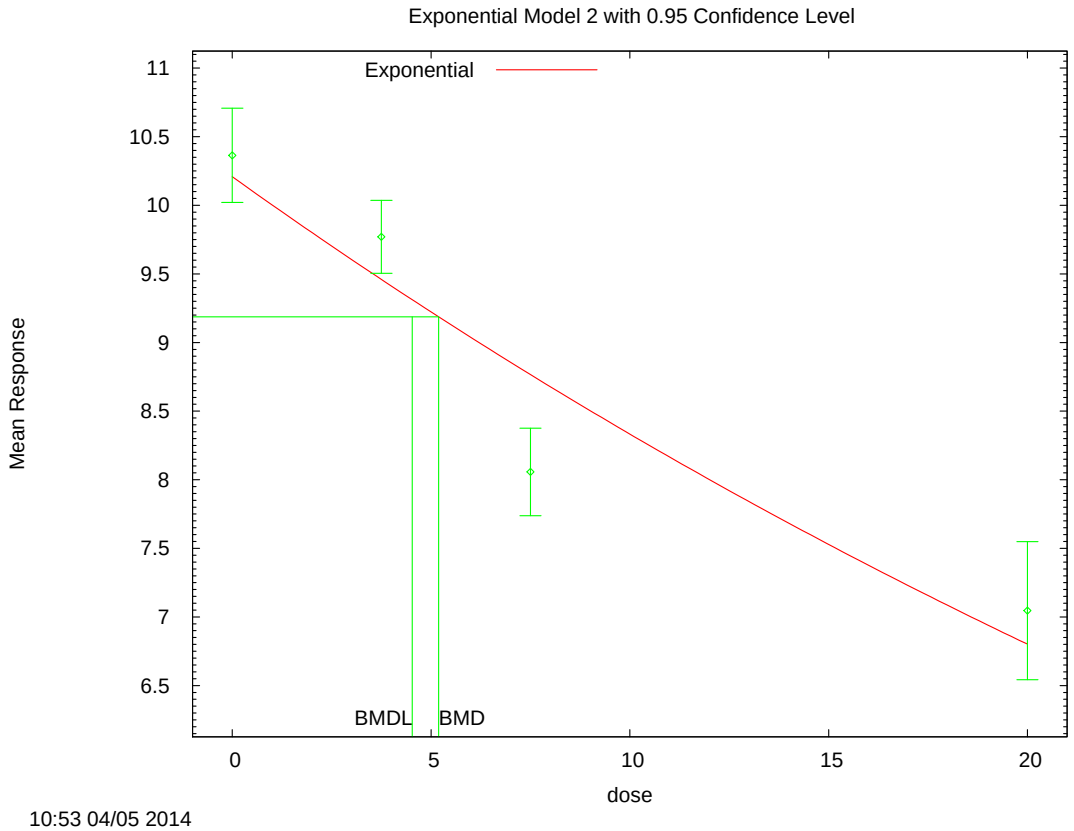
Specified Effect = 0.100000

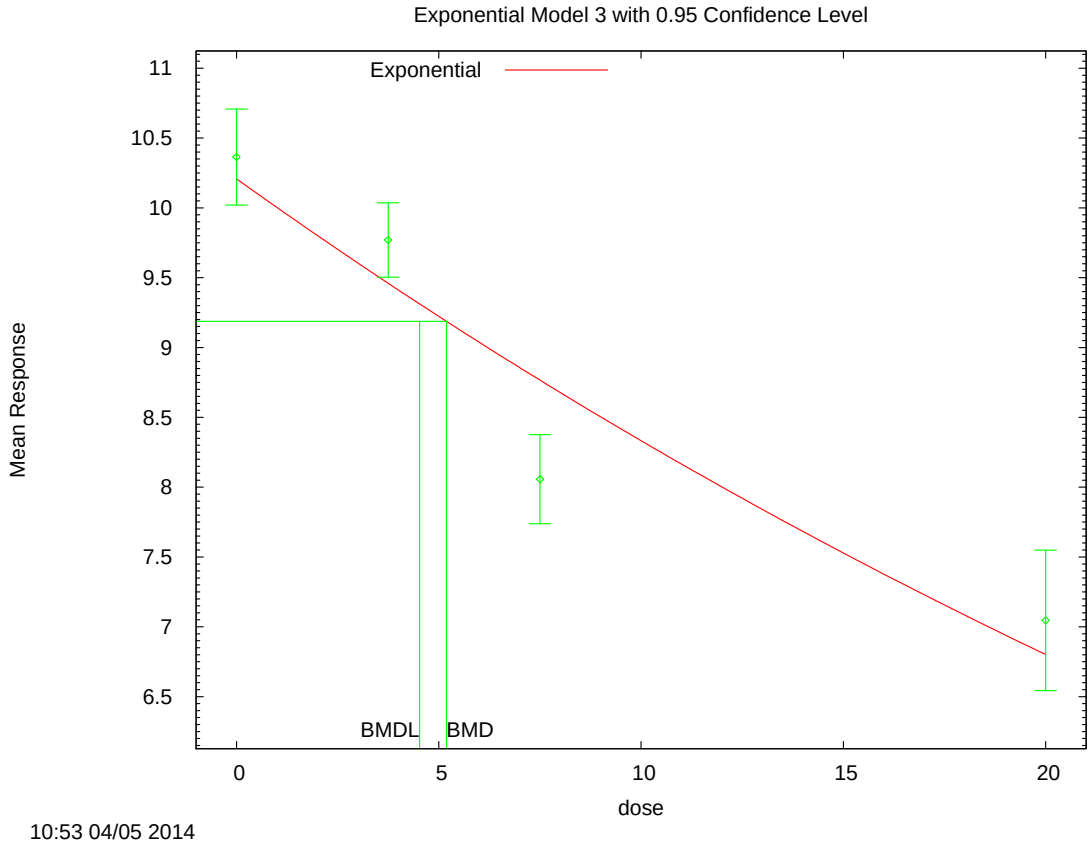
Risk Type = Relative deviation

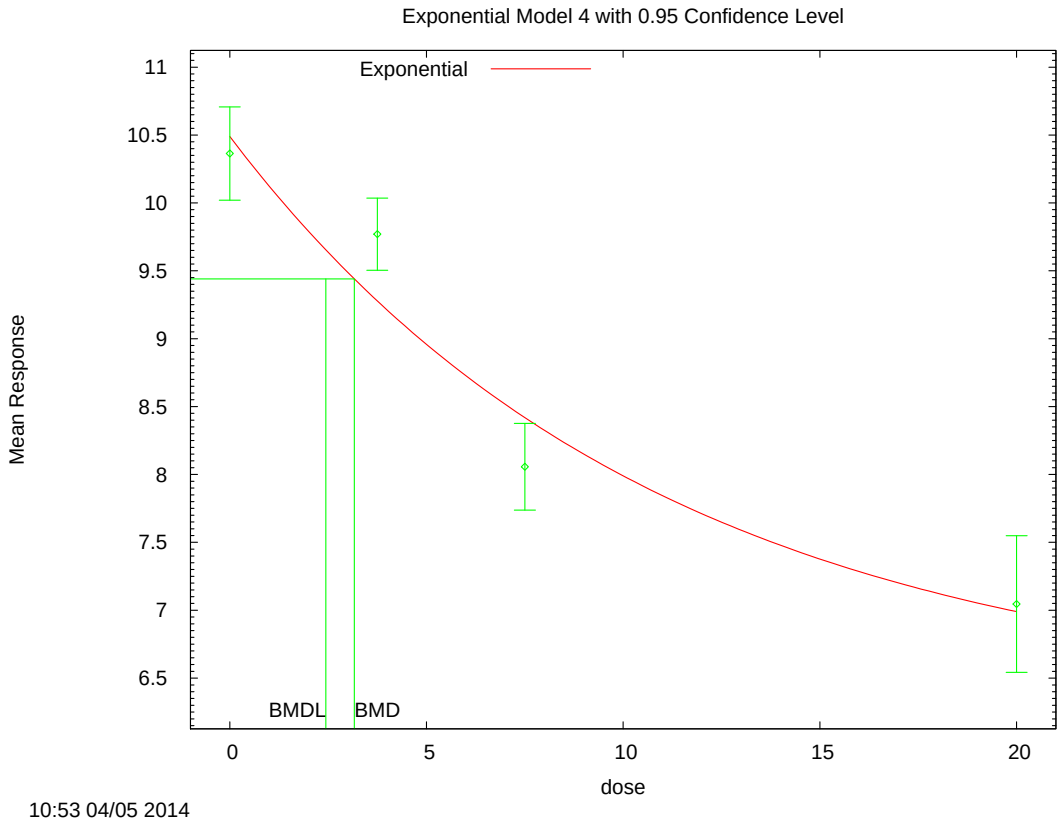
Confidence Level = 0.950000

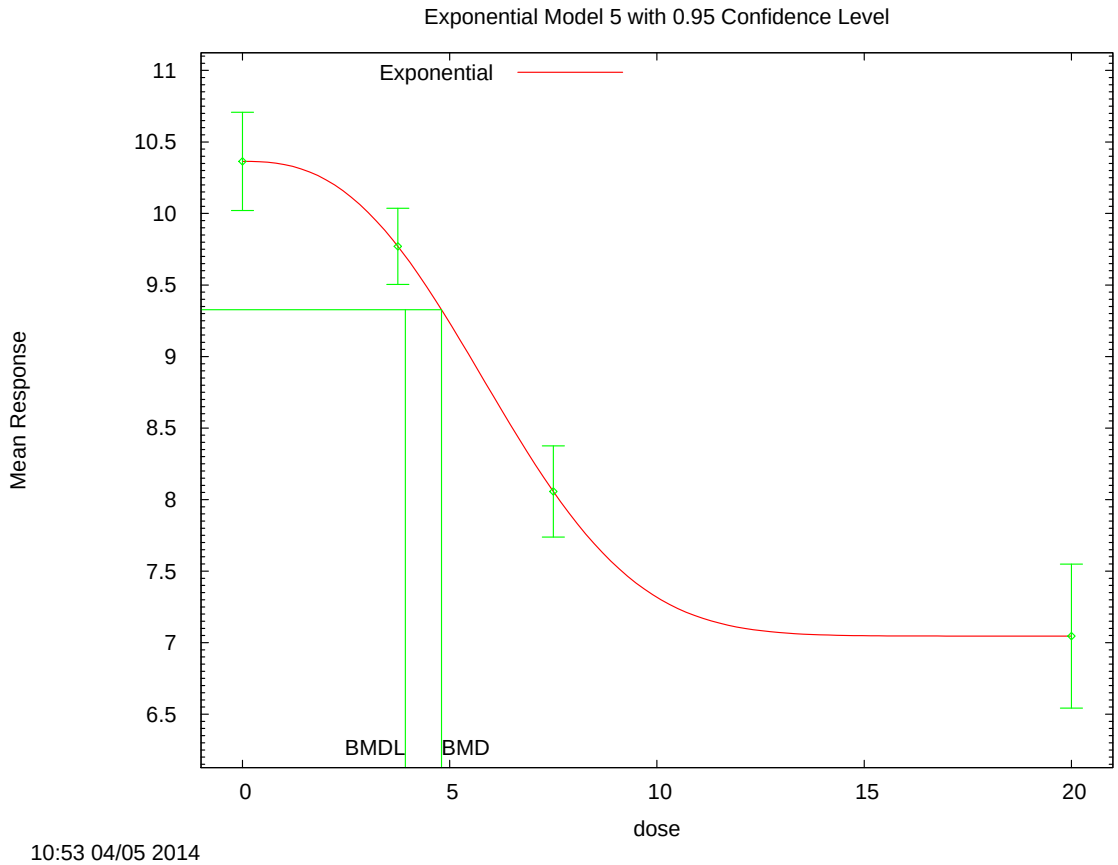
BMD and BMDL by Model

Model	BMD	BMDL
2	5.1908	4.52706
3	5.1908	4.52706
4	3.16618	2.44179
5	4.80267	3.92868


Exponential Model 2 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
11
10.5
10
9.5
9
8.5
8
7.5
7
6.5
0
5
10
15
20
10:53 04/05 2014


Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
11
10.5
10
9.5
9
8.5
8
7.5
7
6.5
0
5
10
15
20
10:53 04/05 2014


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
11
10.5
10
9.5
9
8.5
8
7.5
7
6.5
0
5
10
15
20
10:53 04/05 2014


Exponential Model 5 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
11
10.5
10
9.5
9
8.5
8
7.5
7
6.5
0
5
10
15
20
10:53 04/05 2014

MRID 49037406 Repeat CCA Female Pup PND21 Brain
CONSTANT VARIANCE - NO

```
 ================================================================
        Exponential Model. (Version: 1.7;  Date: 12/10/2009)
        Input Data File: C:/Users/EHolman/Desktop/HED Desktop/BMDS220/Data/exp_Repeat
CCA Female Pup PND21 Brain_Setting.(d)
        Gnuplot Plotting File:
                                              Sat Apr 05 12:10:53 2014
 ================================================================

 BMDS Model Run
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   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log(mean(i)) * rho)

   Total number of dose groups = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 250
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha           7.26578           7.26578             7.26578           7.26578
         rho          -3.80936          -3.80936            -3.80936          -3.80936
           a           7.49819            3.7173             11.0754           11.0754
           b         0.0205491        -0.0033659            0.127436          0.127436
           c                --                --                0.597893
0.597893
           d                --                 2                  --                 1


                               Parameter Estimates by Model

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
```

lnalpha	7.11098	7.11098	7.02777	7.12793
rho	-3.7485	-3.7485	-3.72855	-3.79227
a	10.4896	10.4896	10.5786	10.5445
b	0.0235512	0.0235512	0.0617034	0.114695
c	--	--	0.508515	0.647421
d	--	1	--	1.52428

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	10	10.55	0.452
3.75	10	9.644	0.49
7.5	10	8.494	0.595
20	10	6.953	0.986

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	10.49	0.4275	0.4317
	3.75	9.603	0.5045	0.2573
	7.5	8.791	0.5953	-1.579
	20	6.549	1.034	1.235
3	0	10.49	0.4275	0.4317
	3.75	9.603	0.5045	0.2573
	7.5	8.791	0.5953	-1.579
	20	6.549	1.034	1.235
4	0	10.58	0.4133	-0.2345
	3.75	9.505	0.5046	0.8734
	7.5	8.653	0.6011	-0.8338
	20	6.893	0.9184	0.2068
5	0	10.54	0.4055	0.02725
	3.75	9.647	0.4801	-0.01858
	7.5	8.506	0.6095	-0.06095
	20	6.934	0.8978	0.06672

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-1.593554	5	13.18711
A2	2.514368	8	10.97126
A3	2.394025	6	7.211949

R	-35.81062	2	75.62124
2	0.1948919	4	7.610216
3	0.1948919	4	7.610216
4	1.617474	5	6.765052
5	2.394025	6	7.211949

Additive constant for all log-likelihoods = -36.76. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	76.65	6	< 0.0001
Test 2	8.216	3	0.04176
Test 3	0.2407	2	0.8866
Test 4	4.398	2	0.1109
Test 5a	4.398	2	0.1109
Test 5b	-1.042e-013	0	N/A
Test 6a	1.553	1	0.2127
Test 6b	2.845	1	0.09165
Test 7a	-6.395e-014	0	N/A
Test 7b	4.398	2	0.1109
Test 7c	1.553	1	0.2127

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is greater than .1. Model 2 seems to adequately describe the data.

The p-value for Test 5a is greater than .1. Model 3 seems to adequately describe the data.

Degrees of freedom for Test 5b are less than or equal to 0.
The Chi-Square test for fit is not valid.

The p-value for Test 6a is greater than .1. Model 4 seems
to adequately describe the data.

The p-value for Test 6b is greater than .05. Model 4 does
not seem to fit the data better than Model 2.

Degrees of freedom for Test 7a are less than or equal to 0.
The Chi-Square test for fit is not valid.

The p-value for Test 7b is greater than .05. Model 5 does
not seem to fit the data better than Model 3.

The p-value for Test 7c is greater than .05. Model 5 does
not seem to fit the data better than Model 4.

Benchmark Dose Computations:

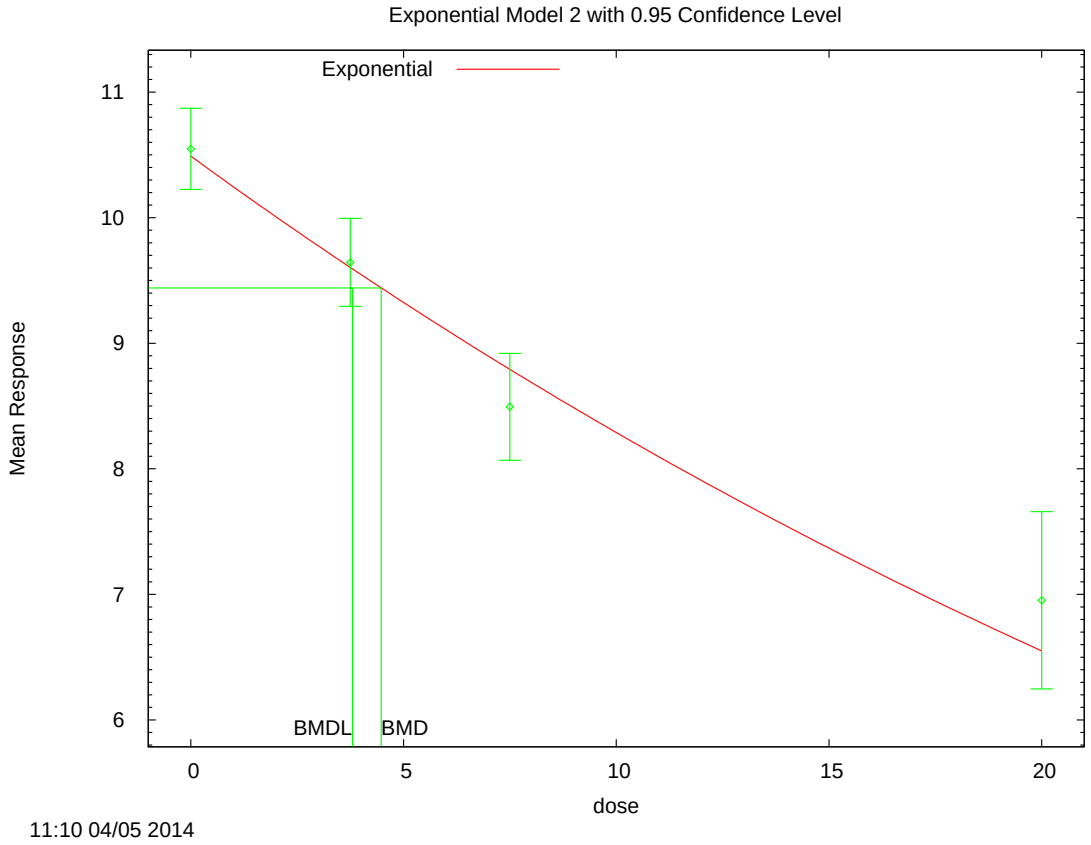
Specified Effect = 0.100000

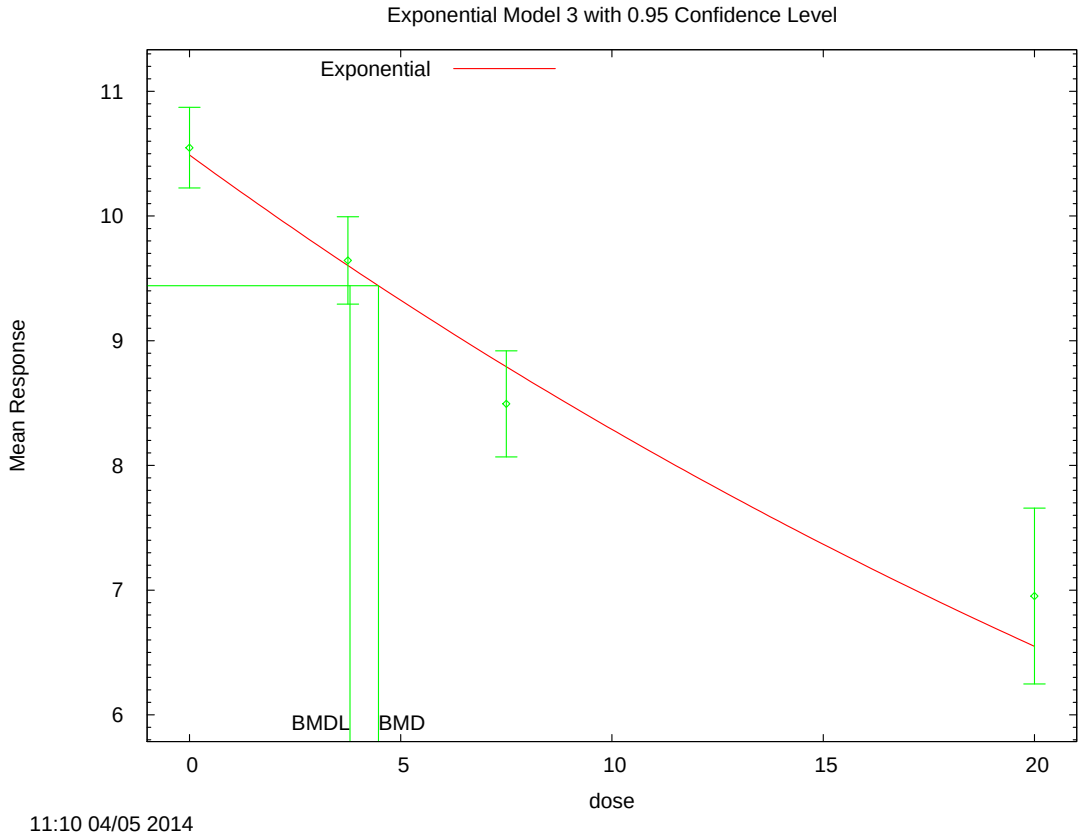
Risk Type = Relative deviation

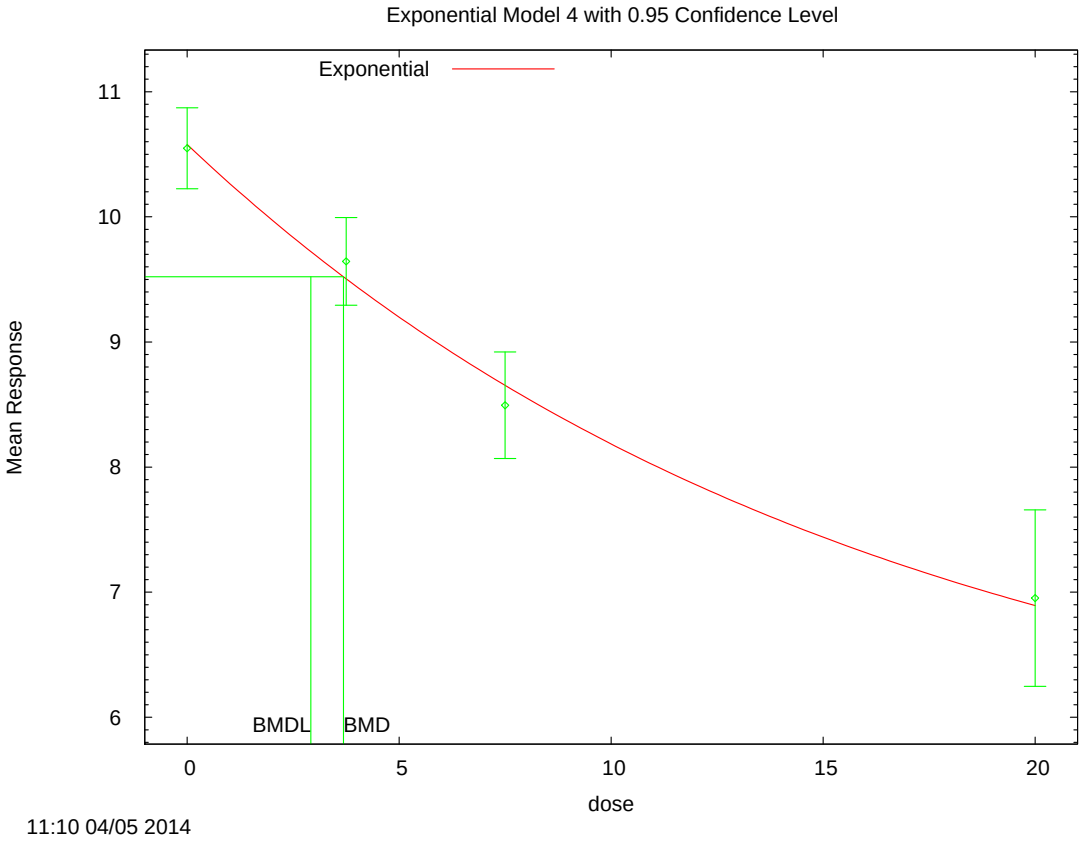
Confidence Level = 0.950000

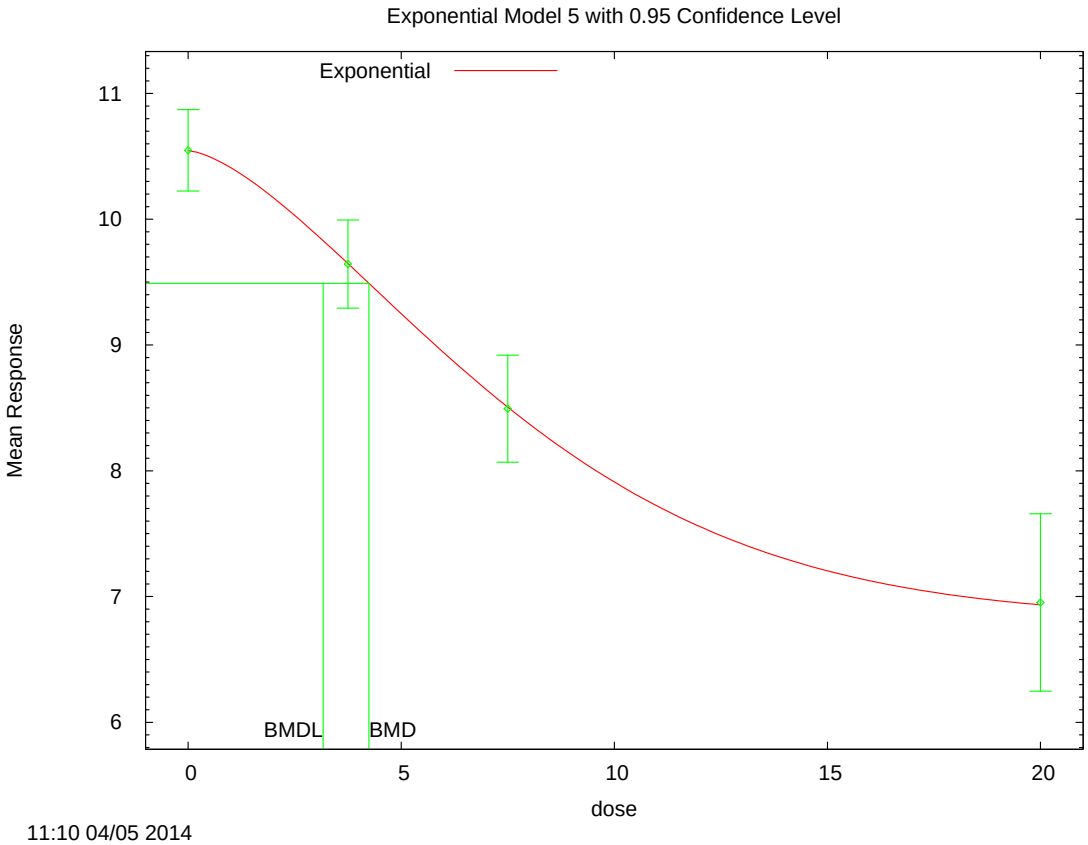
BMD and BMDL by Model

Model	BMD	BMDL
2	4.47368	3.80019
3	4.47368	3.80019
4	3.68674	2.91878
5	4.24253	3.16751


Exponential Model 2 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
11:10 04/05 2014


Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
11:10 04/05 2014


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
11
10
9
8
7
6
0
5
10
15
20
11:10 04/05 2014


Exponential Model 5 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
BMD
11
10
9
8
7
6
0
5
10
15
20
11:10 04/05 2014

MRID 43608201 -Subchronic Neurotoxicity Male Adult RBC ChE – Week 3
CONSTANT VARIANCE - YES

```
 ================================================================
        Exponential Model. (Version: 1.7;  Date: 12/10/2009)
        Input Data File: C:/Users/EHolman/Desktop/HED Desktop/BMDS220/Data/exp_Subchr
Neuro Male RBC Week 3_Setting.(d)
        Gnuplot Plotting File:
                                              Sat Apr 05 12:34:46 2014
 ================================================================

 BMDS Model Run
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   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 250
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha           10.4913           10.4913             10.4913           10.4913
         rho(S)              0                 0                   0                 0
           a           1393.26           1393.26             2105.25           2105.25
           b         0.0278769         0.0278769            0.145079          0.145079
           c                --                --                0.488574
0.488574
           d                --                 1                  --                 1

     (S) = Specified
```

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	10.6718	10.6718	10.503	10.4928
rho	0	0	0	0
a	1939.41	1939.41	2010.88	1994.5
b	0.0287671	0.0287671	0.19867	0.414494
c	--	--	0.529829	0.541489
d	--	1	--	6.34154

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	5	1984	123.2
0.2	5	2005	199.8
2.1	5	1684	209.8
21.1	5	1080	284.4

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	1939	207.7	0.4801
	0.2	1928	207.7	0.826
	2.1	1826	207.7	-1.526
	21.1	1057	207.7	0.2481
3	0	1939	207.7	0.4801
	0.2	1928	207.7	0.826
	2.1	1826	207.7	-1.526
	21.1	1057	207.7	0.2481
4	0	2011	190.9	-0.3149
	0.2	1974	190.9	0.3627
	2.1	1688	190.9	-0.05116
	21.1	1080	190.9	0.003374
5	0	1995	189.9	-0.1237
	0.2	1994	189.9	0.1237
	2.1	1684	189.9	-3.443e-007
	21.1	1080	189.9	1.641e-007

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC

A1	-114.9126	5	239.8252
A2	-113.3069	8	242.6138
A3	-114.9126	5	239.8252
R	-130.7509	2	265.5017
2	-116.7178	3	239.4356
3	-116.7178	3	239.4356
4	-115.03	4	238.0599
5	-114.9279	5	239.8558

Additive constant for all log-likelihoods = -18.38. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	34.89	6	< 0.0001
Test 2	3.211	3	0.3602
Test 3	3.211	3	0.3602
Test 4	3.61	2	0.1644
Test 5a	3.61	2	0.1644
Test 5b	-1.99e-013	0	N/A
Test 6a	0.2347	1	0.6281
Test 6b	3.376	1	0.06617
Test 7a	0.0306	0	N/A
Test 7b	3.58	2	0.167
Test 7c	0.2041	1	0.6514

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is greater than .1. A homogeneous variance model appears to be appropriate here.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is greater than .1. Model 2 seems to adequately describe the data.

The p-value for Test 5a is greater than .1. Model 3 seems to adequately describe the data.

Degrees of freedom for Test 5b are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

The p-value for Test 6b is greater than .05. Model 4 does not seem to fit the data better than Model 2.

Degrees of freedom for Test 7a are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 7b is greater than .05. Model 5 does not seem to fit the data better than Model 3.

The p-value for Test 7c is greater than .05. Model 5 does not seem to fit the data better than Model 4.

Benchmark Dose Computations:

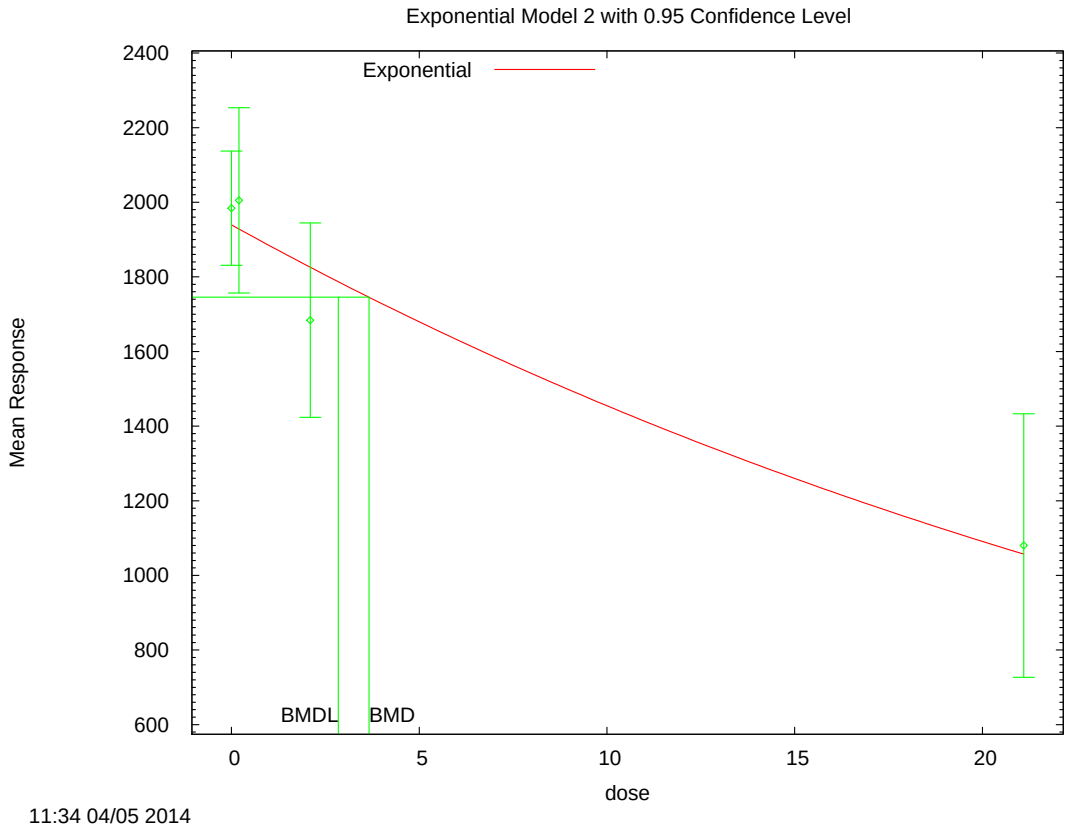
Specified Effect = 0.100000

Risk Type = Relative deviation

Confidence Level = 0.950000

BMD and BMDL by Model

Model	BMD	BMDL
2	3.66253	2.84576
3	3.66253	2.84576
4	1.20366	0.678565
5	1.93395	0.692593



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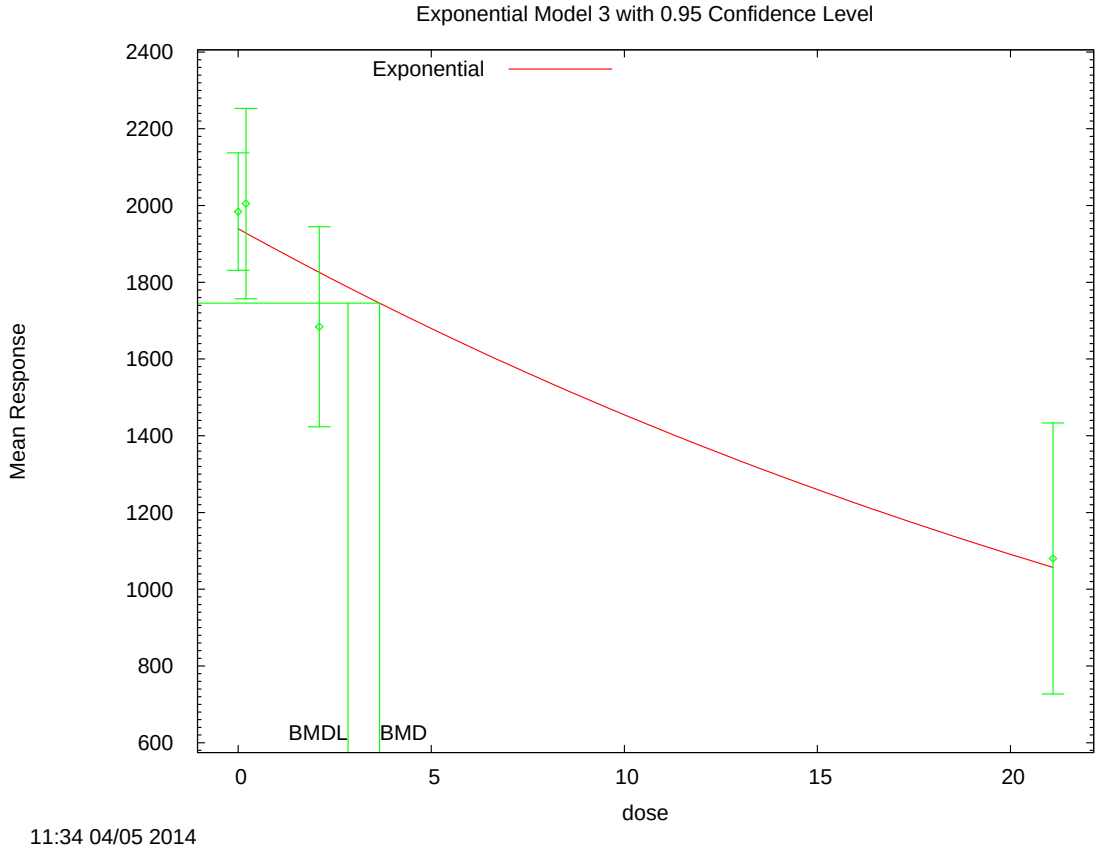

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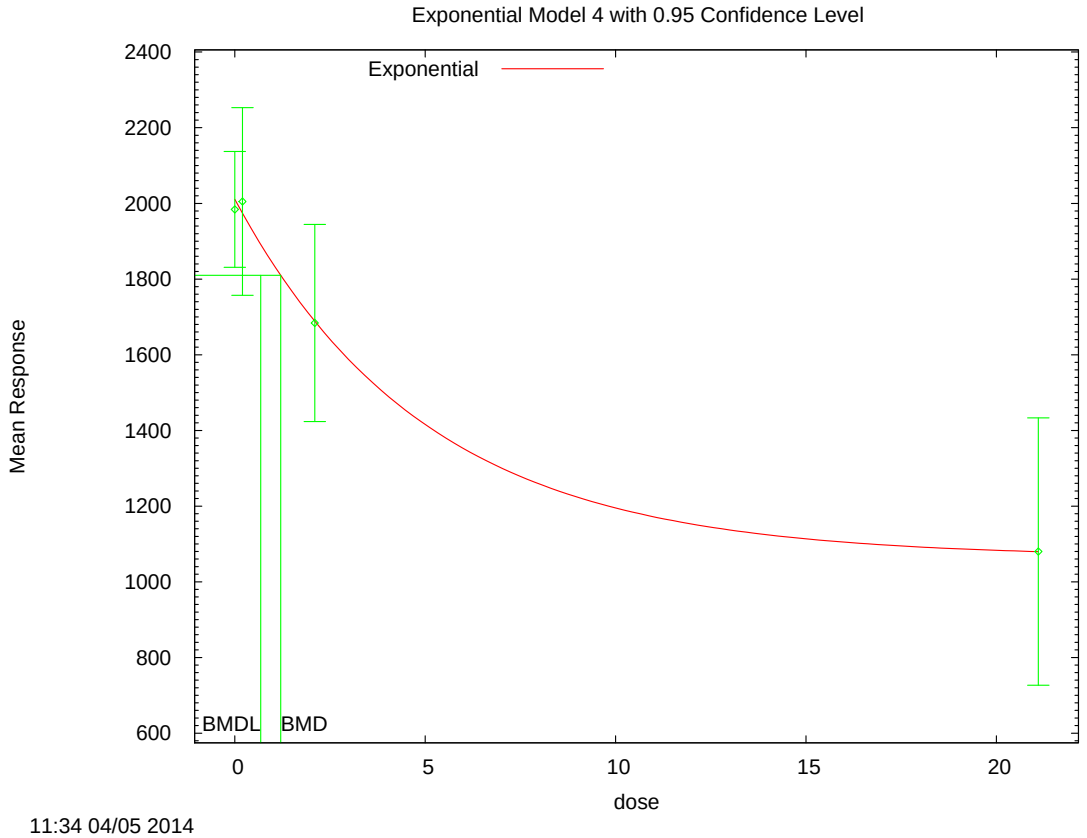
Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
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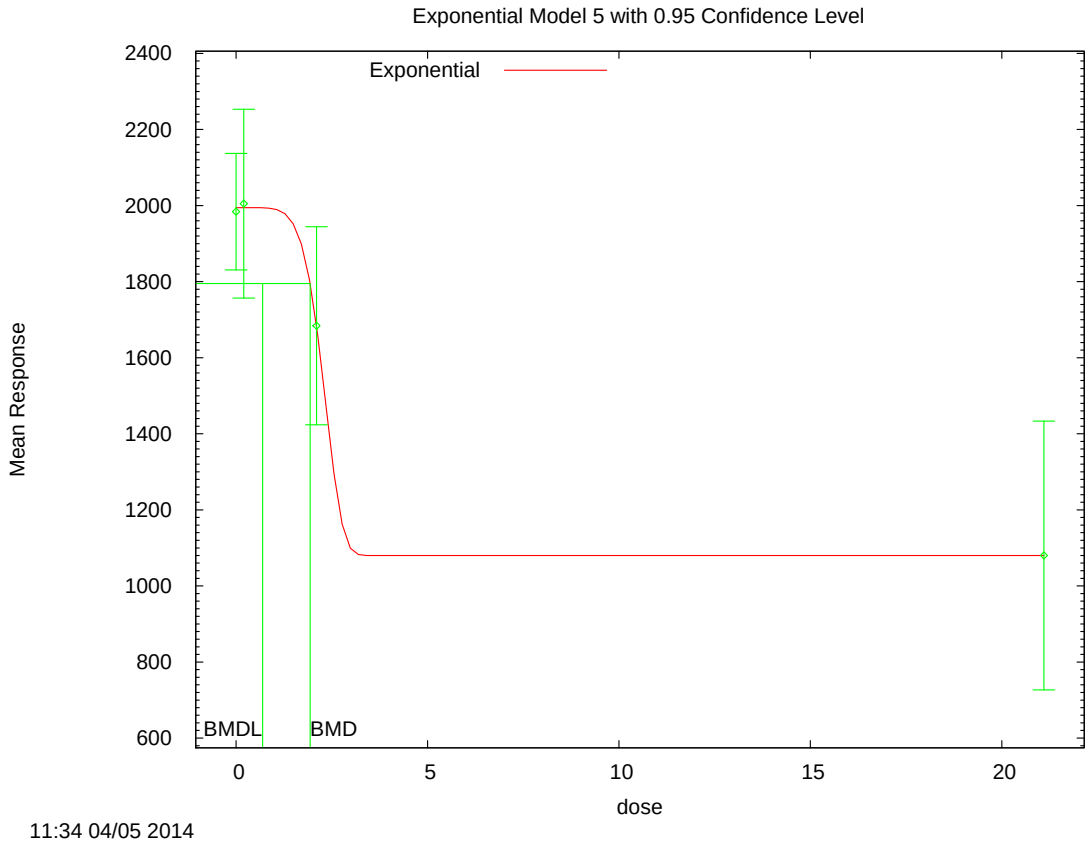
Exponential Model 5 with 0.95 Confidence Level
Exponential
Mean Response
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MRID 43608201 -Subchronic Neurotoxicity Female RBC ChE – Week 7
CONSTANT VARIANCE - YES

```
 ======================================================================
        Exponential Model. (Version: 1.7;  Date: 12/10/2009)
        Input Data File: C:/Users/EHolman/Desktop/HED Desktop/BMDS220/Data/exp_Subchr
Neuro Female RBC Week 7_Setting.(d)
        Gnuplot Plotting File:
                                              Sat Apr 05 13:45:46 2014
 ======================================================================

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 250
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha           10.4962           10.4962             10.4962           10.4962
         rho(S)              0                 0                   0                 0
           a           1433.36           1433.36             2172.45           2172.45
           b         0.0238803         0.0238803            0.124273          0.124273
           c                --                --                0.48486
0.48486
           d                --                 1                  --                 1

     (S) = Specified
```

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	10.5911	10.5911	10.5107	10.5107
rho	0	0	0	0
a	1991.03	1991.03	2038.47	2038.47
b	0.0243573	0.0243573	0.1258	0.1258
c	--	--	0.521231	0.521231
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	5	2069	155.2
0.2	5	1980	259.1
2.4	5	1788	200.3
24.7	5	1106	222.6

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	1991	199.4	0.8741
	0.2	1981	199.4	-0.01523
	2.4	1878	199.4	-1.009
	24.7	1091	199.4	0.169
3	0	1991	199.4	0.8741
	0.2	1981	199.4	-0.01523
	2.4	1878	199.4	-1.009
	24.7	1091	199.4	0.169
4	0	2038	191.6	0.3563
	0.2	2014	191.6	-0.3994
	2.4	1784	191.6	0.04509
	24.7	1106	191.6	-0.001911
5	0	2038	191.6	0.3563
	0.2	2014	191.6	-0.3994
	2.4	1784	191.6	0.04509
	24.7	1106	191.6	-0.001912

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC

A1	-114.9621	5	239.9242
A2	-114.3042	8	244.6083
A3	-114.9621	5	239.9242
R	-130.9338	2	265.8676
2	-115.911	3	237.822
3	-115.911	3	237.822
4	-115.1074	4	238.2148
5	-115.1074	4	238.2148

Additive constant for all log-likelihoods = -18.38. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	33.26	6	< 0.0001
Test 2	1.316	3	0.7254
Test 3	1.316	3	0.7254
Test 4	1.898	2	0.3872
Test 5a	1.898	2	0.3872
Test 5b	-2.842e-013	0	N/A
Test 6a	0.2906	1	0.5898
Test 6b	1.607	1	0.2049
Test 7a	0.2906	1	0.5898
Test 7b	1.607	1	0.2049
Test 7c	2.842e-014	0	N/A

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is greater than .1. A homogeneous variance model appears to be appropriate here.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is greater than .1. Model 2 seems to adequately describe the data.

The p-value for Test 5a is greater than .1. Model 3 seems to adequately describe the data.

Degrees of freedom for Test 5b are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

The p-value for Test 6b is greater than .05. Model 4 does not seem to fit the data better than Model 2.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

The p-value for Test 7b is greater than .05. Model 5 does not seem to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0. The Chi-Square test for fit is not valid.

Benchmark Dose Computations:

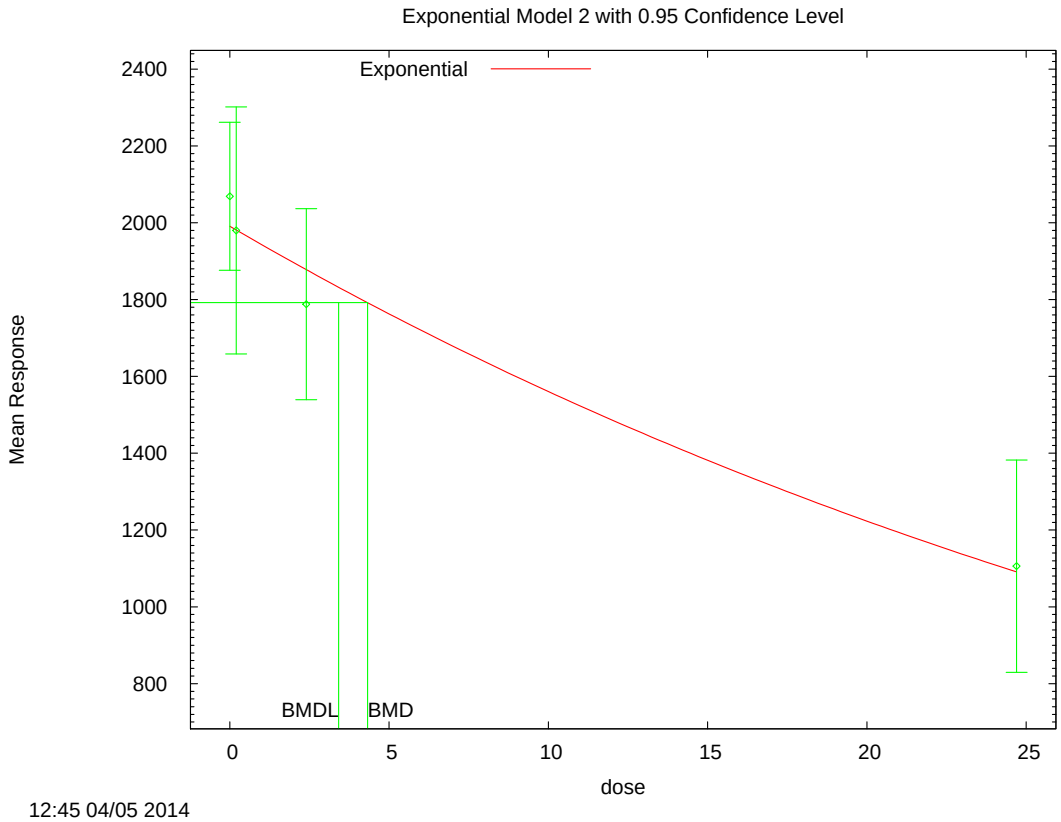
Specified Effect = 0.100000

Risk Type = Relative deviation

Confidence Level = 0.950000

BMD and BMDL by Model

Model	BMD	BMDL
2	4.32563	3.41479
3	4.32563	3.41479
4	1.86241	0.964064
5	1.86241	0.964064


Exponential Model 2 with 0.95 Confidence Level
Exponential
Mean Response
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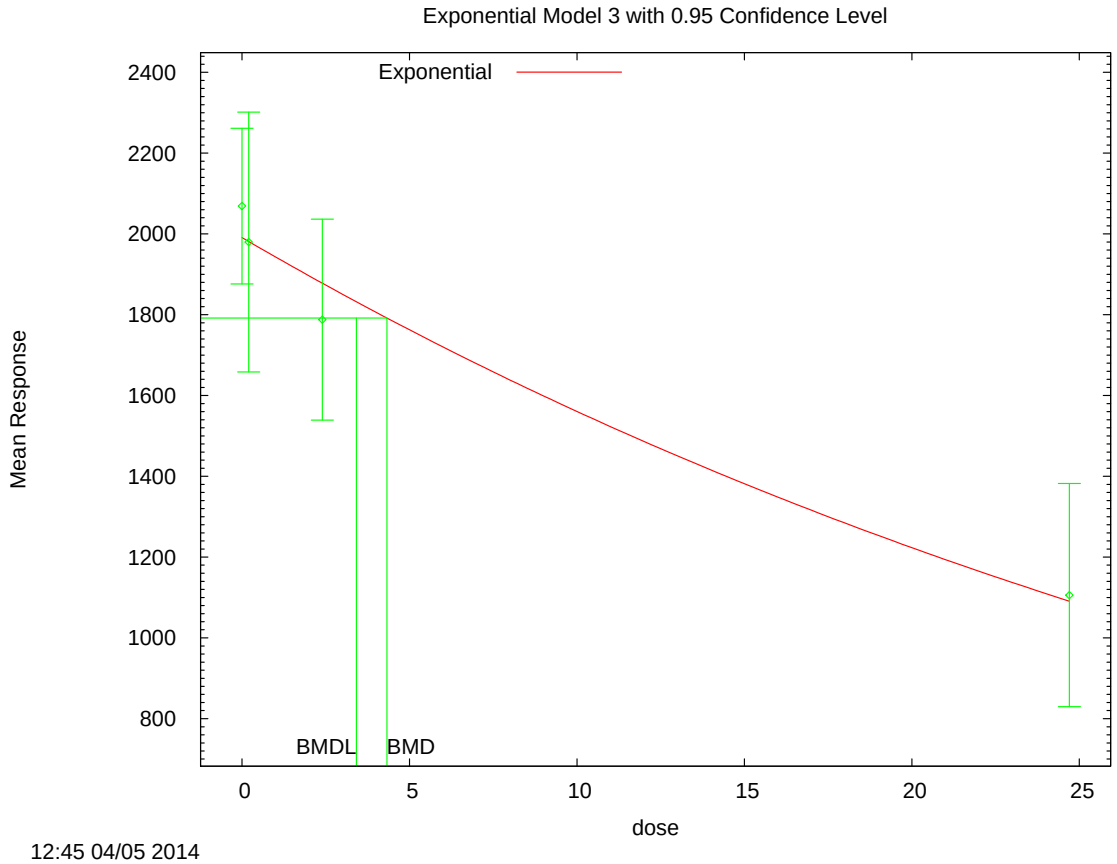
Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
dose
BMDL
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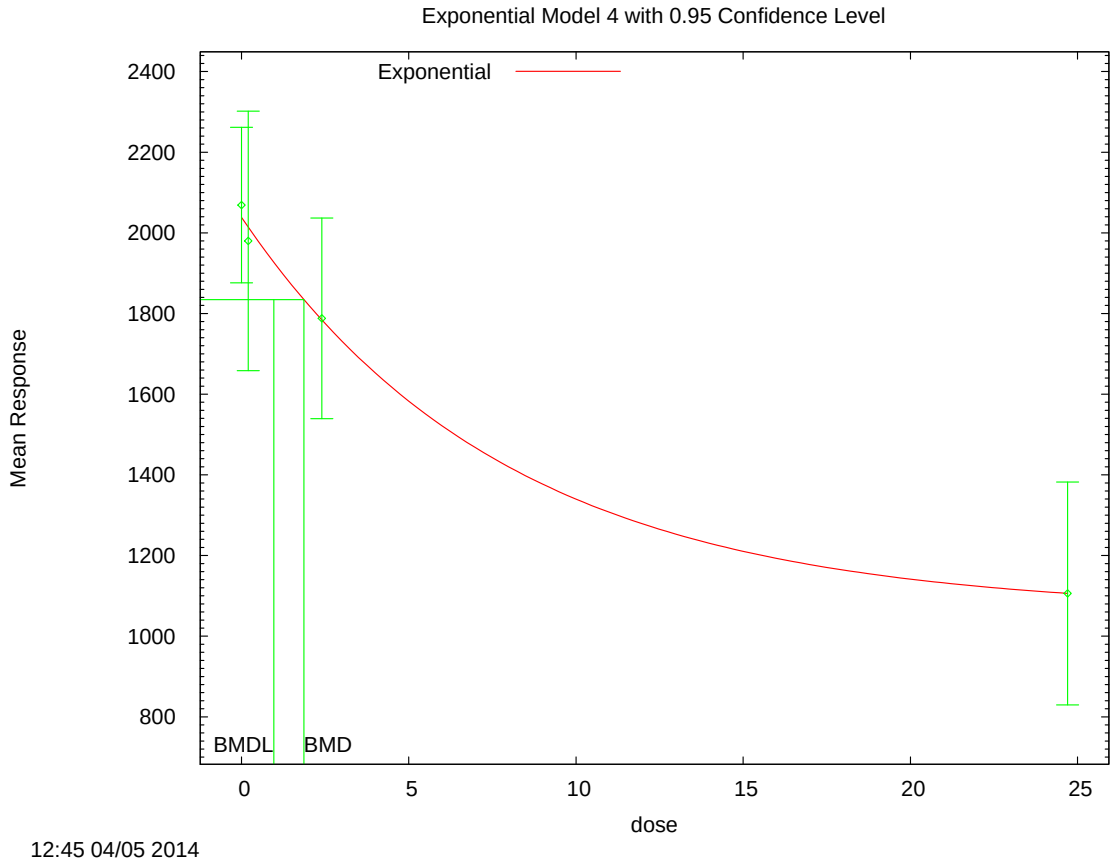
Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
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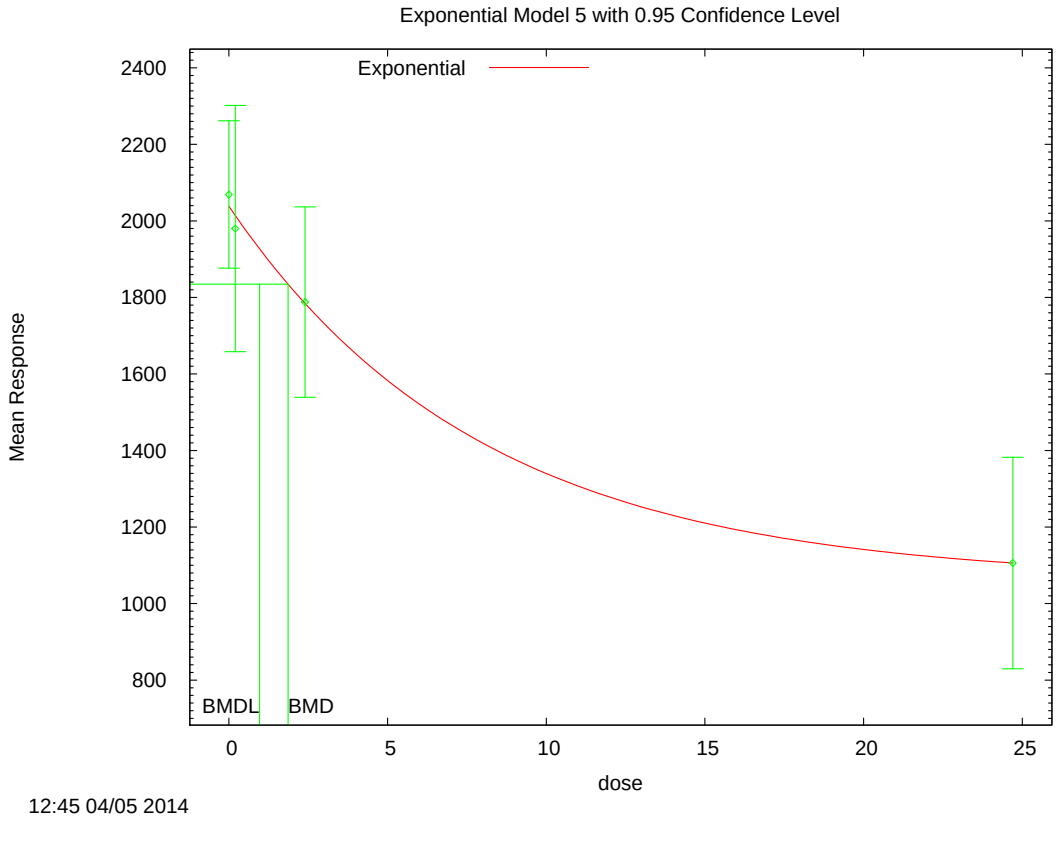
Exponential Model 5 with 0.95 Confidence Level
Exponential
Mean Response
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MRID 43608201 -Subchronic Neurotoxicity Male Adult RBC ChE – Week 13
CONSTANT VARIANCE - YES

```
 ================================================================
        Exponential Model. (Version: 1.7;  Date: 12/10/2009)
        Input Data File: C:/Users/EHolman/Desktop/HED Desktop/BMDS220/Data/exp_Subchr
Neuro Male RBC Week 13_Setting.(d)
        Gnuplot Plotting File:
                                              Sat Apr 05 12:49:08 2014
 ================================================================

 BMDS Model Run
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   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 250
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha             10.65             10.65             10.65             10.65
         rho(S)              0                 0                 0                 0
           a           1598.16           1598.16           2192.4            2192.4
           b         0.0227203         0.0227203          0.130267          0.130267
           c                --                --          0.559943
0.559943
           d                --                 1                --                 1

     (S) = Specified
```

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	10.6637	10.6556	10.6637	10.6549
rho	0	0	0	0
a	2083.98	2067.63	2083.98	2067.5
b	0.0226056	0.0263938	0.0226056	0.318574
c	--	--	0	0.623458
d	--	1.28039	--	6.62214

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	5	2047	230.9
0.2	5	2088	288.4
2.1	5	2015	239.6
21.1	5	1289	130.6

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	2084	206.8	-0.3998
	0.2	2075	206.8	0.1451
	2.1	1987	206.8	0.2989
	21.1	1293	206.8	-0.04791
3	0	2068	206	-0.224
	0.2	2065	206	0.2483
	2.1	2017	206	-0.02528
	21.1	1289	206	0.001041
4	0	2084	206.8	-0.3998
	0.2	2075	206.8	0.1451
	2.1	1987	206.8	0.2989
	21.1	1293	206.8	-0.04791
5	0	2068	205.9	-0.2226
	0.2	2067	205.9	0.2226
	2.1	2015	205.9	-4.775e-008
	21.1	1289	205.9	-6.427e-010

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC

A1	-116.4996	5	242.9991
A2	-115.0558	8	246.1116
A3	-116.4996	5	242.9991
R	-129.2798	2	262.5596
2	-116.6368	3	239.2735
3	-116.556	4	241.1119
4	-116.6368	3	239.2735
5	-116.5492	5	243.0985

Additive constant for all log-likelihoods = -18.38. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	28.45	6	< 0.0001
Test 2	2.888	3	0.4093
Test 3	2.888	3	0.4093
Test 4	0.2744	2	0.8718
Test 5a	0.1128	1	0.737
Test 5b	0.1616	1	0.6877
Test 6a	0.2744	2	0.8718
Test 6b	0	0	N/A
Test 7a	0.09936	0	N/A
Test 7b	0.01342	1	0.9078
Test 7c	0.175	2	0.9162

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is greater than .1. A homogeneous variance model appears to be appropriate here.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is greater than .1. Model 2 seems to adequately describe the data.

The p-value for Test 5a is greater than .1. Model 3 seems to adequately describe the data.

The p-value for Test 5b is greater than .05. Model 3 does not seem to fit the data better than Model 2.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

Degrees of freedom for Test 6b are less than or equal to 0. The Chi-Square test for fit is not valid.

Degrees of freedom for Test 7a are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 7b is greater than .05. Model 5 does not seem to fit the data better than Model 3.

The p-value for Test 7c is greater than .05. Model 5 does not seem to fit the data better than Model 4.

Benchmark Dose Computations:

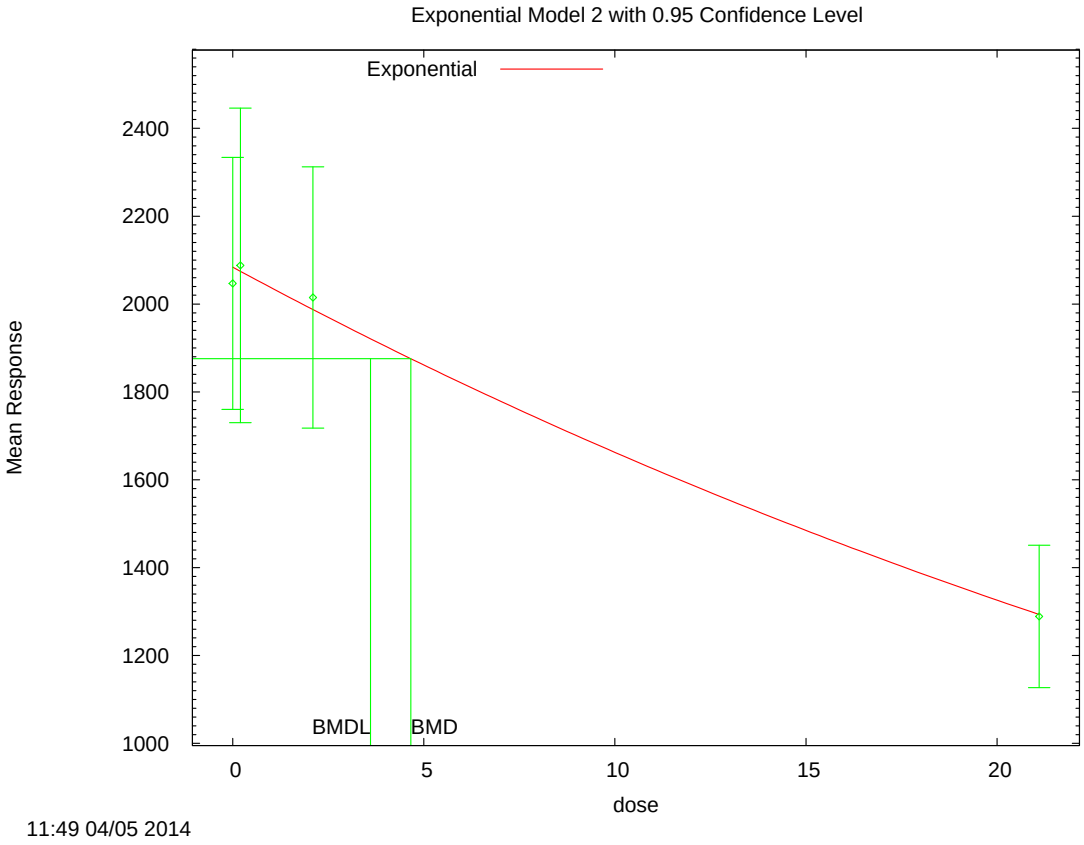
Specified Effect = 0.100000

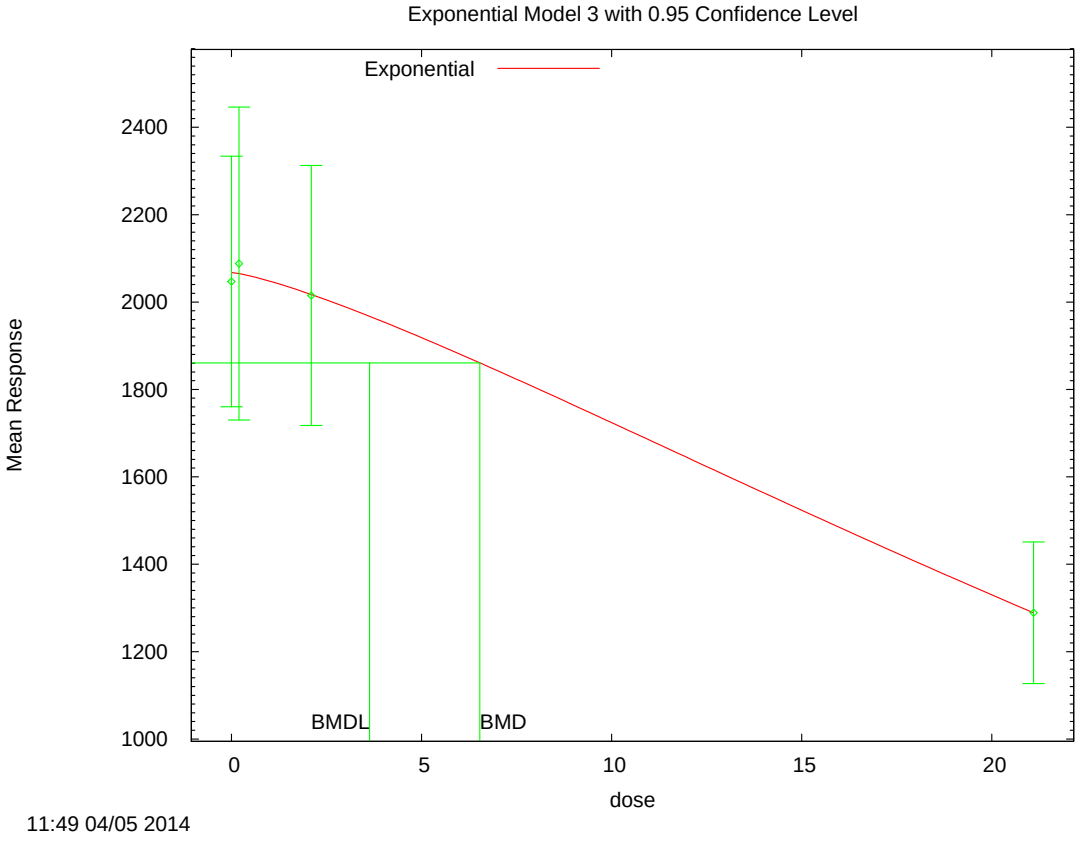
Risk Type = Relative deviation

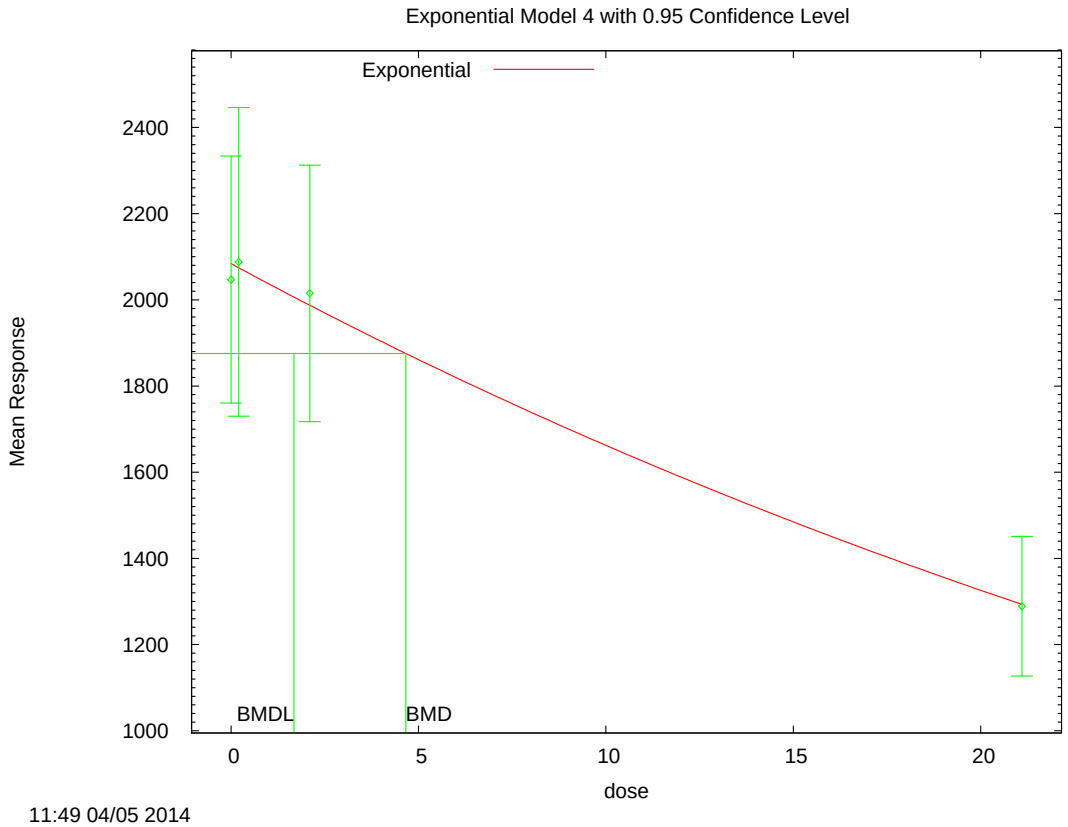
Confidence Level = 0.950000

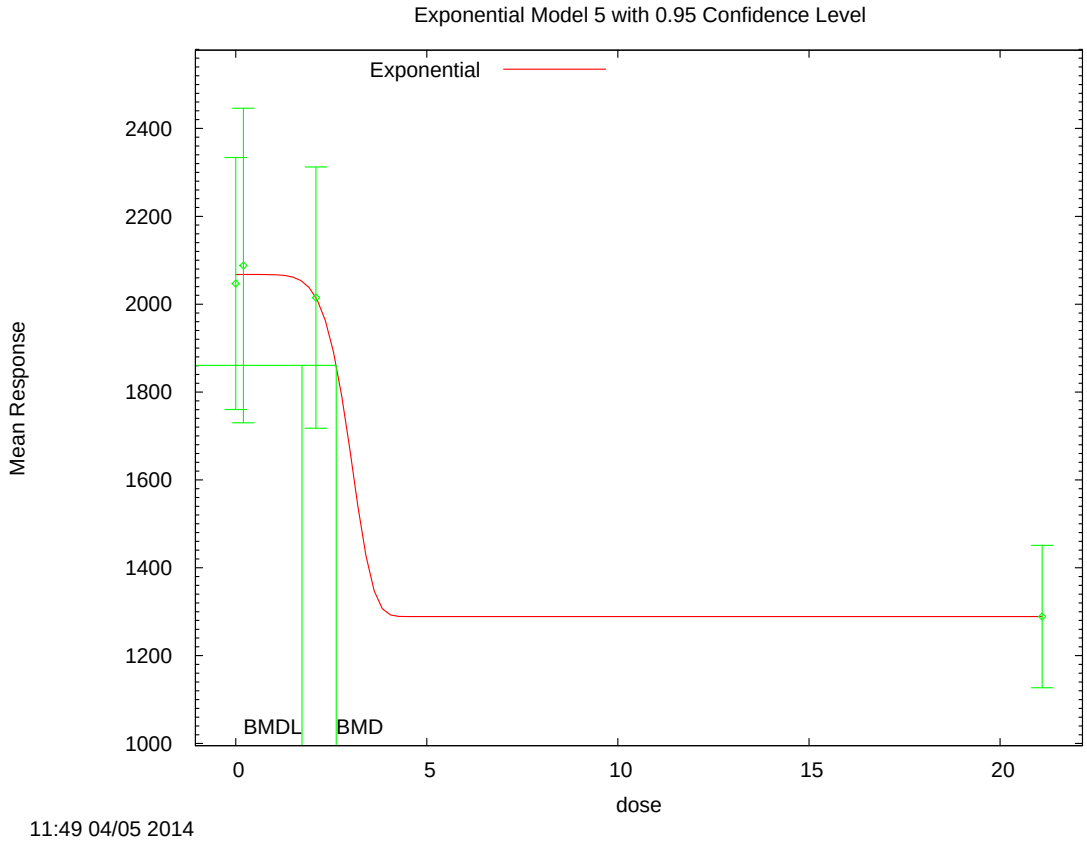
BMD and BMDL by Model

Model	BMD	BMDL
2	4.66081	3.60491
3	6.53429	3.63292
4	4.66081	1.67912
5	2.62844	1.73243


Exponential Model 2 with 0.95 Confidence Level
Exponential
Mean Response
2400
2200
2000
1800
1600
1400
1200
1000
BMDL
BMD
0
5
10
15
20
dose
11:49 04/05 2014


Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
2400
2200
2000
1800
1600
1400
1200
1000
BMDL
BMD
0
5
10
15
20
dose
11:49 04/05 2014


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
2400
2200
2000
1800
1600
1400
1200
1000
BMDL
BMD
0
5
10
15
20
dose
11:49 04/05 2014


Exponential Model 5 with 0.95 Confidence Level
Exponential
Mean Response
2400
2200
2000
1800
1600
1400
1200
1000
BMDL
BMD
0
5
10
15
20
dose
11:49 04/05 2014

MRID 43608201 -Subchronic Neurotoxicity Female Adult RBC ChE – Week 7
CONSTANT VARIANCE - YES

```
 ================================================================
        Exponential Model. (Version: 1.7;  Date: 12/10/2009)
        Input Data File: C:/Users/EHolman/Desktop/HED Desktop/BMDS220/Data/exp_Subchr
Neuro Female RBC Week 13_Setting.(d)
        Gnuplot Plotting File:
                                              Sat Apr 05 13:58:04 2014
 ================================================================

 BMDS Model Run
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   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 250
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha           10.8339           10.8339             10.8339           10.8339
         rho(S)              0                 0                   0                 0
           a           1557.98           1557.98           2157.75           2157.75
           b         0.0190804         0.0190804             0.11211           0.11211
           c                --                --                0.5579
0.5579
           d                --                 1                  --                 1

     (S) = Specified
```

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	10.845	10.845	10.836	10.836
rho	0	0	0	0
a	2022.9	2022.9	2041.31	2041.31
b	0.0192058	0.0192058	0.0697633	0.0697632
c	--	--	0.536488	0.536488
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	5	2055	270.1
0.2	5	2013	241.5
2.4	5	1897	250.2
24.7	5	1264	244.3

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	2023	226.4	0.317
	0.2	2015	226.4	-0.02118
	2.4	1932	226.4	-0.3434
	24.7	1259	226.4	0.05148
3	0	2023	226.4	0.317
	0.2	2015	226.4	-0.02118
	2.4	1932	226.4	-0.3434
	24.7	1259	226.4	0.05148
4	0	2041	225.4	0.1358
	0.2	2028	225.4	-0.1508
	2.4	1895	225.4	0.01541
	24.7	1264	225.4	-0.0003479
5	0	2041	225.4	0.1358
	0.2	2028	225.4	-0.1508
	2.4	1895	225.4	0.01541
	24.7	1264	225.4	-0.0003479

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC

A1	-118.3391	5	246.6783
A2	-118.3002	8	252.6003
A3	-118.3391	5	246.6783
R	-129.3449	2	262.6897
2	-118.4505	3	242.901
3	-118.4505	3	242.901
4	-118.3599	4	244.7197
5	-118.3599	4	244.7197

Additive constant for all log-likelihoods = -18.38. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	22.09	6	0.001167
Test 2	0.07794	3	0.9943
Test 3	0.07794	3	0.9943
Test 4	0.2227	2	0.8946
Test 5a	0.2227	2	0.8946
Test 5b	-1.137e-013	0	N/A
Test 6a	0.04145	1	0.8387
Test 6b	0.1812	1	0.6703
Test 7a	0.04145	1	0.8387
Test 7b	0.1812	1	0.6703
Test 7c	2.842e-014	0	N/A

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is greater than .1. A homogeneous variance model appears to be appropriate here.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is greater than .1. Model 2 seems to adequately describe the data.

The p-value for Test 5a is greater than .1. Model 3 seems to adequately describe the data.

Degrees of freedom for Test 5b are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

The p-value for Test 6b is greater than .05. Model 4 does not seem to fit the data better than Model 2.

The p-value for Test 7a is greater than .1. Model 5 seems to adequately describe the data.

The p-value for Test 7b is greater than .05. Model 5 does not seem to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0. The Chi-Square test for fit is not valid.

Benchmark Dose Computations:

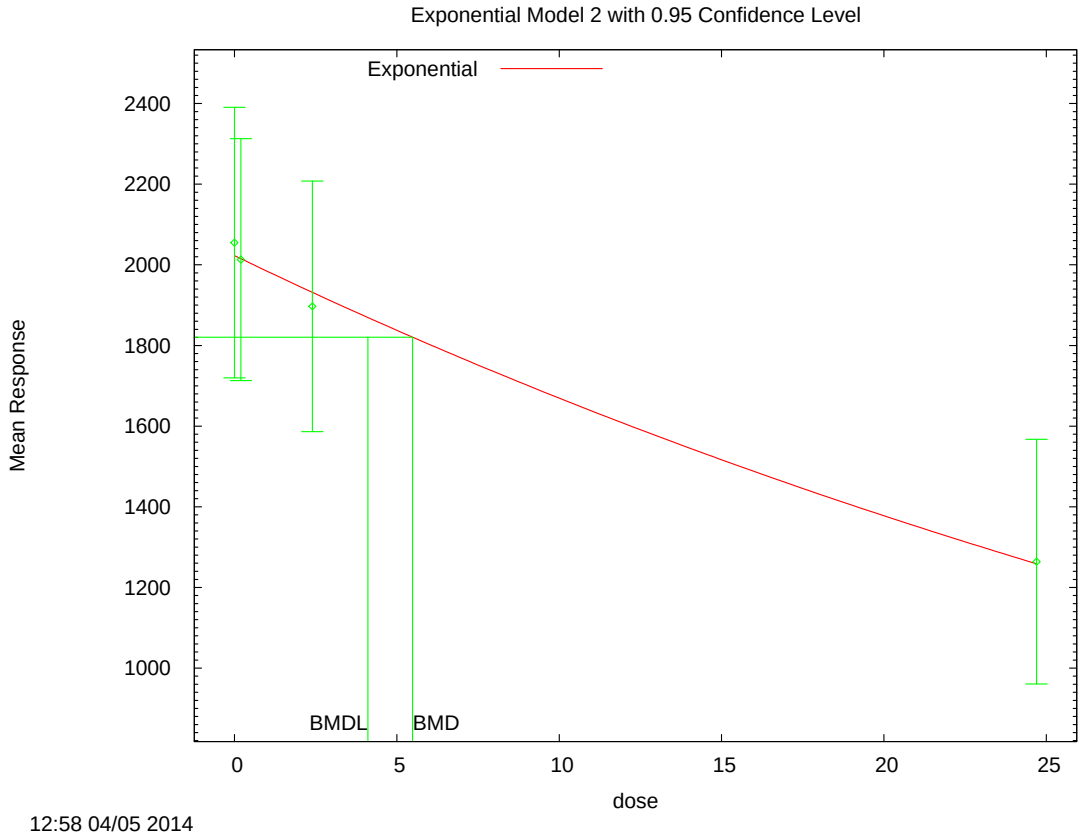
Specified Effect = 0.100000

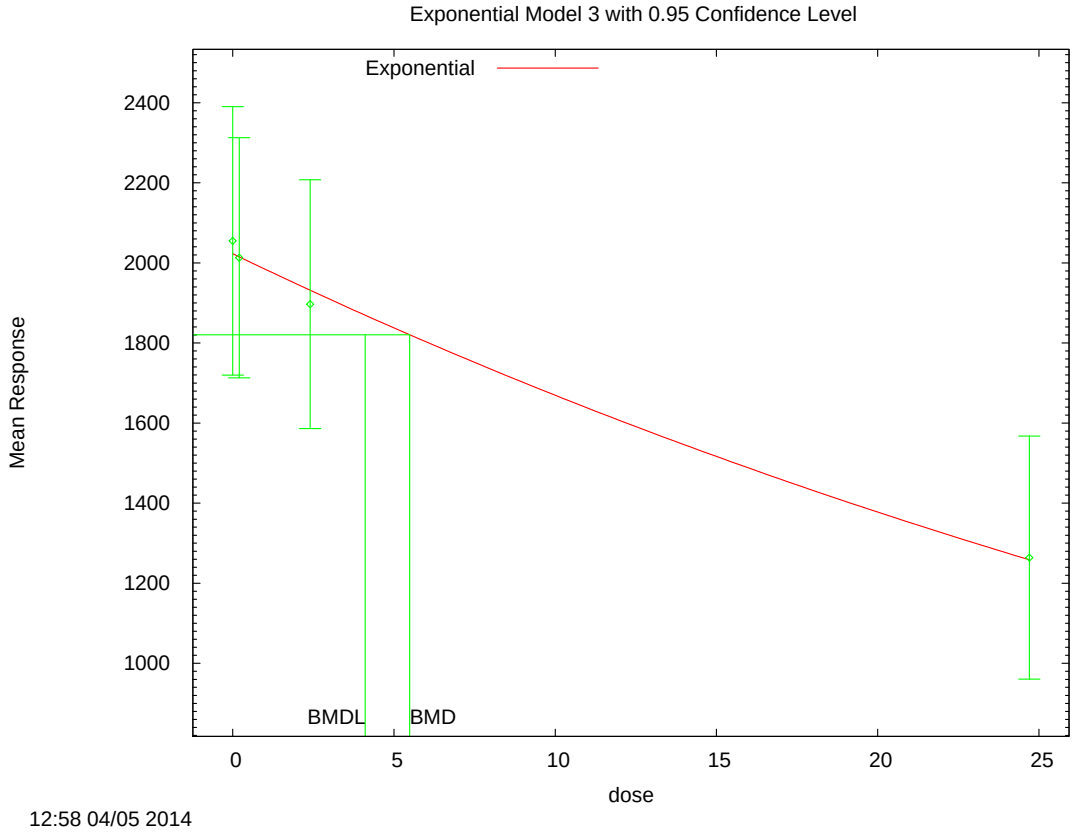
Risk Type = Relative deviation

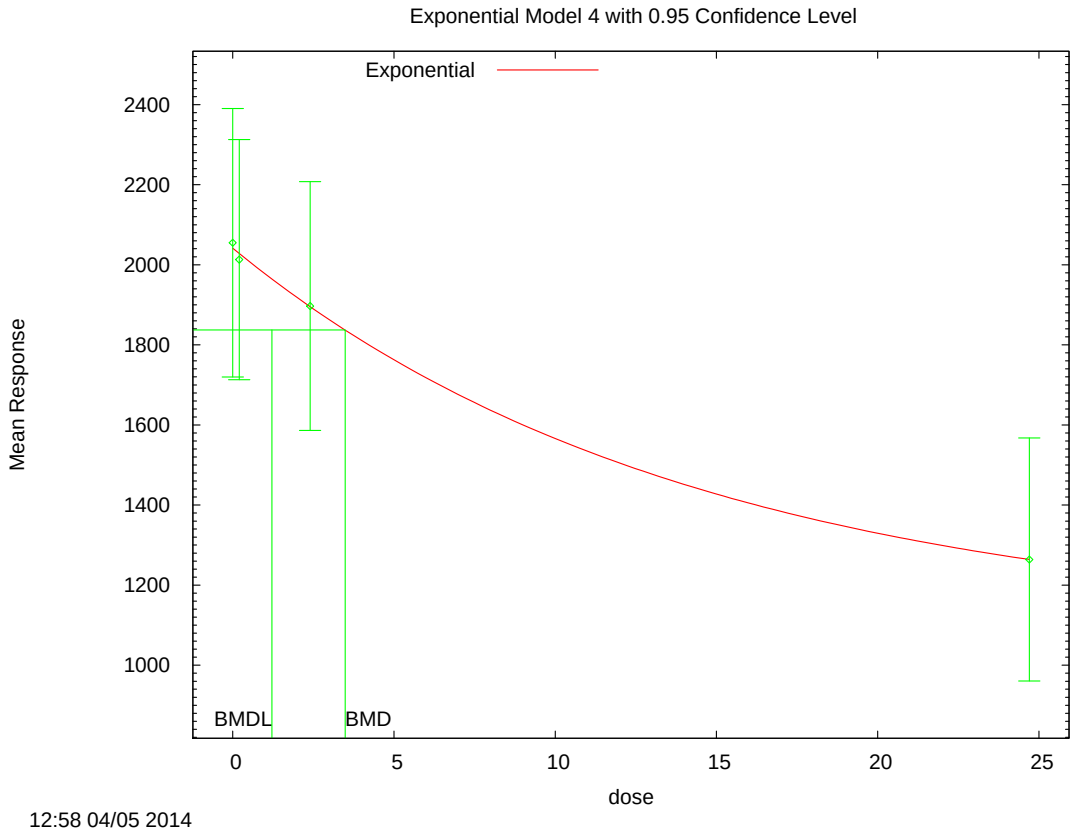
Confidence Level = 0.950000

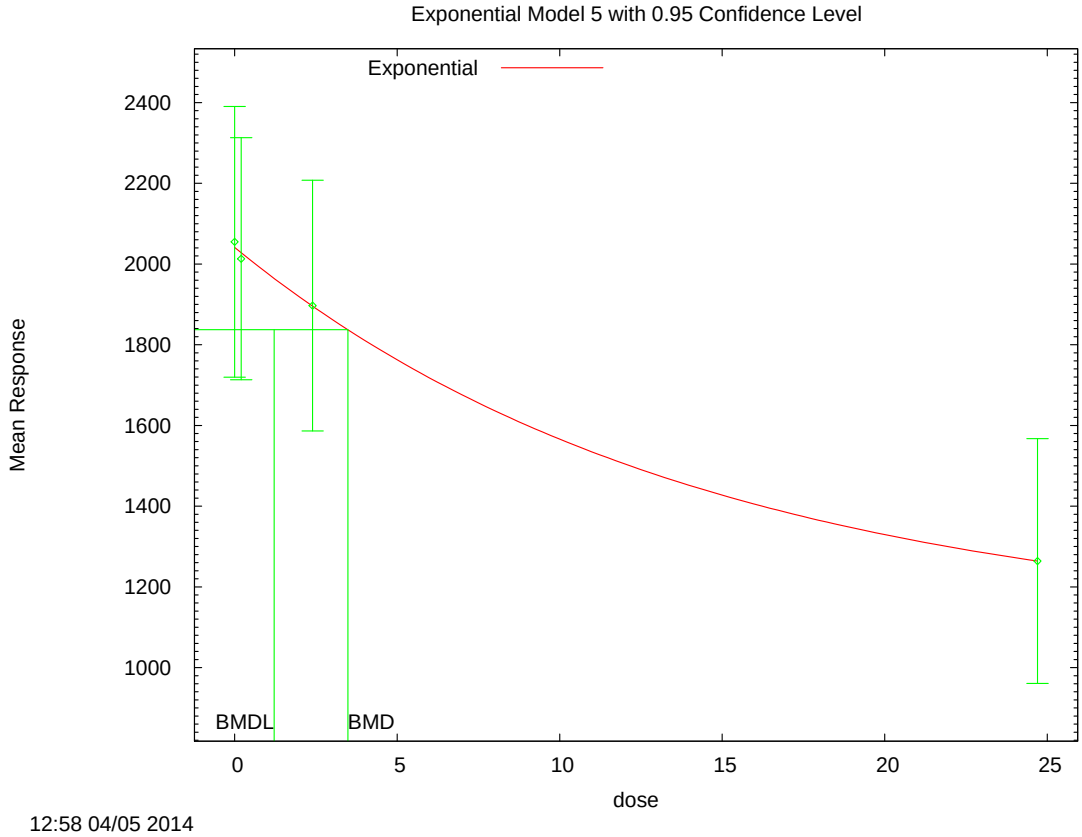
BMD and BMDL by Model

Model	BMD	BMDL
2	5.48586	4.10919
3	5.48586	4.10919
4	3.4835	1.21265
5	3.4835	1.21265


Exponential Model 2 with 0.95 Confidence Level
Exponential
Mean Response
2400
2200
2000
1800
1600
1400
1200
1000
BMDL
BMD
0
5
10
15
20
25
dose
12:58 04/05 2014


Exponential Model 3 with 0.95 Confidence Level
Exponential
Mean Response
2400
2200
2000
1800
1600
1400
1200
1000
BMDL
BMD
0
5
10
15
20
25
dose
12:58 04/05 2014


Exponential Model 4 with 0.95 Confidence Level
Exponential
Mean Response
2400
2200
2000
1800
1600
1400
1200
1000
BMDL
BMD
0
5
10
15
20
25
dose
12:58 04/05 2014


Exponential Model 5 with 0.95 Confidence Level
Exponential
Mean Response
2400
2200
2000
1800
1600
1400
1200
1000
BMDL
BMD
0
5
10
15
20
25
dose
12:58 04/05 2014

MRID 43608201 -Subchronic Neurotoxicity Male Brainstem
CONSTANT VARIANCE – NO

```
 ======================================================================
        Exponential Model. (Version: 1.7;  Date: 12/10/2009)
        Input Data File: C:/Users/EHolman/Desktop/HED Desktop/BMDS220/Data/exp_Subchr
Neuro Male Brainstem_Setting.(d)
        Gnuplot Plotting File:
                                              Sat Apr 05 13:35:49 2014
 ======================================================================

 BMDS Model Run
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   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log(mean(i)) * rho)

   Total number of dose groups = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 250
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha           8.62268           8.62268             8.62268           8.62268
         rho          -5.26731          -5.26731            -5.26731          -5.26731
           a           7.11029           3.31072               8.988             8.988
           b         0.0124865       -0.00228924            0.109322          0.109322
           c                --                --               0.669676
0.669676
           d                --                 2                    --                 1


                               Parameter Estimates by Model

     Variable          Model 2           Model 3           Model 4           Model 5
```

lnalpha	-10.17	-10.1339	-10.17	-10.02
rho	4.36621	4.34713	4.36621	4.28883
a	8.23471	8.20791	8.23471	8.22059
b	0.0125323	0.015011	0.0125323	0.352653
c	--	--	0	0.768757
d	--	1.16673	--	7.46476

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	5	7.89	0.778
0.2	5	8.56	0.074
2.1	5	8.02	0.681
21.1	5	6.32	0.387

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	8.235	0.6174	-1.248
	0.2	8.214	0.614	1.26
	2.1	8.021	0.5829	-0.003155
	21.1	6.321	0.3466	-0.008521
3	0	8.208	0.6118	-1.162
	0.2	8.199	0.6103	1.324
	2.1	8.064	0.5887	-0.1664
	21.1	6.319	0.3466	0.004213
4	0	8.235	0.6174	-1.248
	0.2	8.214	0.614	1.26
	2.1	8.021	0.5829	-0.003155
	21.1	6.321	0.3466	-0.008521
5	0	8.221	0.6111	-1.21
	0.2	8.221	0.6111	1.242
	2.1	8.029	0.581	-0.03451
	21.1	6.32	0.3477	0.002353

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	4.070768	5	1.858463
A2	13.17265	8	-10.3453

A3	4.172298	6	3.655404
R	-9.386316	2	22.77263
2	2.845542	4	2.308916
3	2.87386	5	4.252281
4	2.845542	4	2.308916
5	2.922235	6	6.15553

Additive constant for all log-likelihoods = -18.38. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	45.12	6	< 0.0001
Test 2	18.2	3	0.0003993
Test 3	18	2	0.0001234
Test 4	2.654	2	0.2653
Test 5a	2.597	1	0.1071
Test 5b	0.05664	1	0.8119
Test 6a	2.654	2	0.2653
Test 6b	1.332e-014	0	N/A
Test 7a	2.5	0	N/A
Test 7b	0.09675	1	0.7558
Test 7c	0.1534	2	0.9262

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 4 is greater than .1. Model 2 seems to adequately describe the data.

The p-value for Test 5a is greater than .1. Model 3 seems to adequately describe the data.

The p-value for Test 5b is greater than .05. Model 3 does not seem to fit the data better than Model 2.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

Degrees of freedom for Test 6b are less than or equal to 0. The Chi-Square test for fit is not valid.

Degrees of freedom for Test 7a are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 7b is greater than .05. Model 5 does not seem to fit the data better than Model 3.

The p-value for Test 7c is greater than .05. Model 5 does not seem to fit the data better than Model 4.

Benchmark Dose Computations:

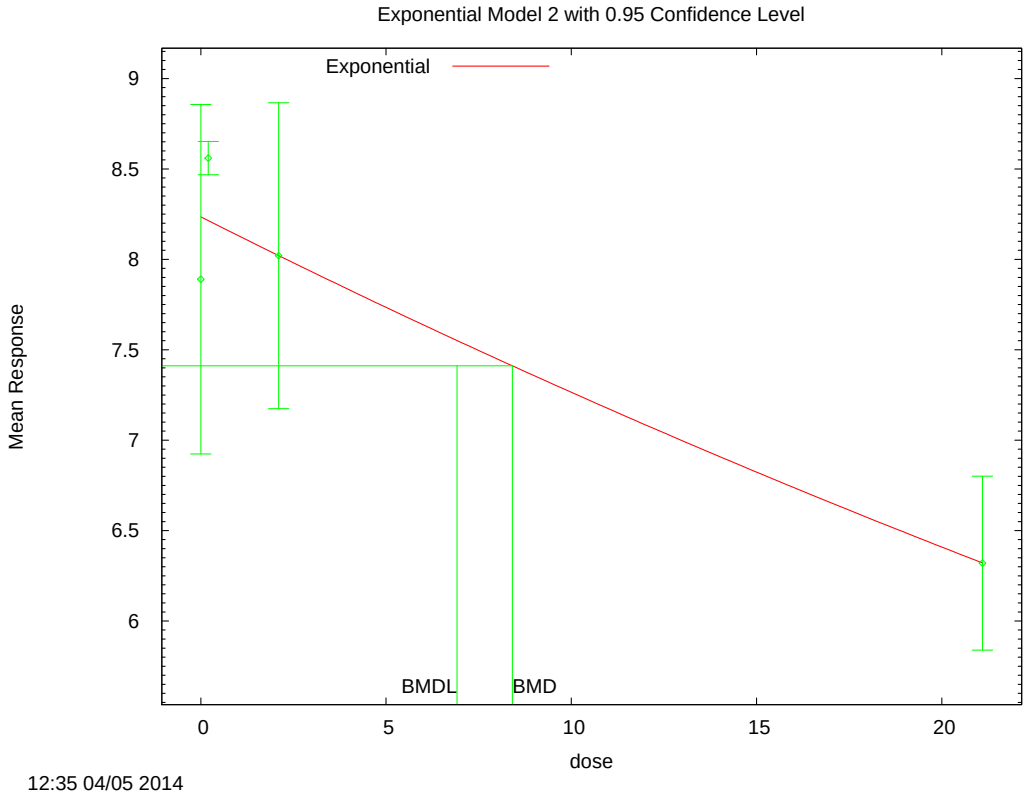
Specified Effect = 0.100000

Risk Type = Relative deviation

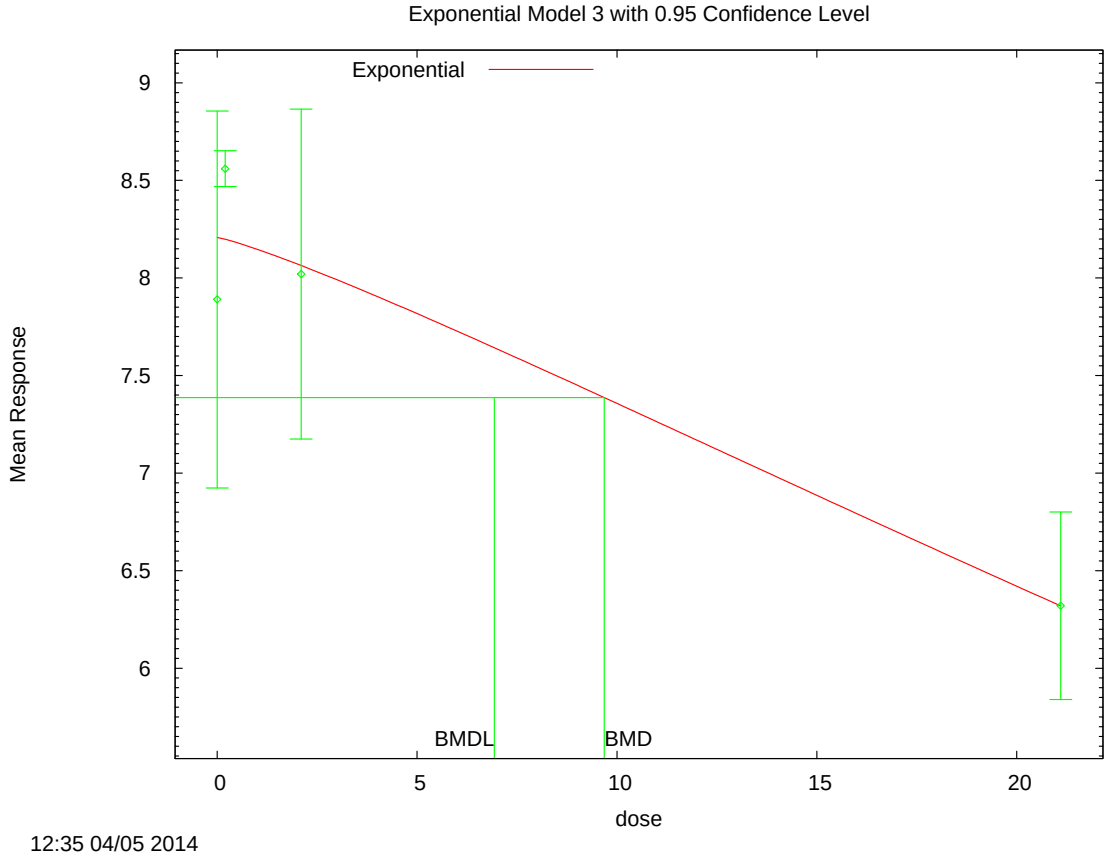
Confidence Level = 0.950000

BMD and BMDL by Model

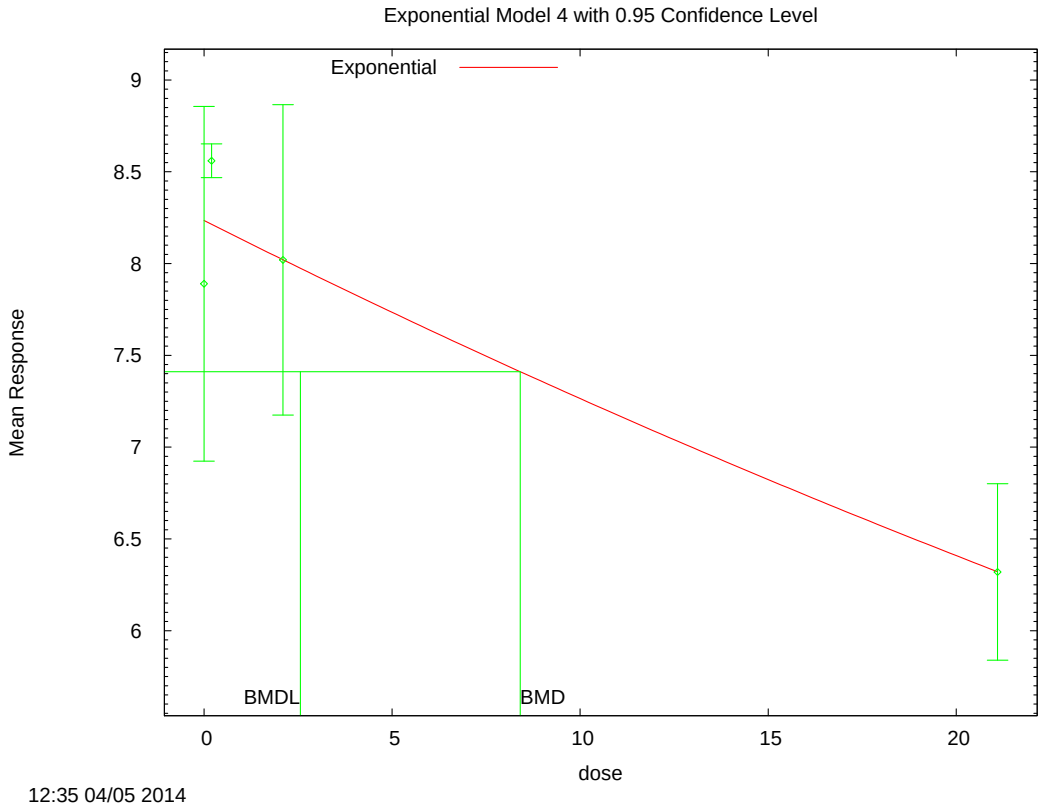
Model	BMD	BMDL
2	8.40715	6.9147
3	9.68122	6.92979
4	8.40715	2.56087
5	2.62774	2.12533



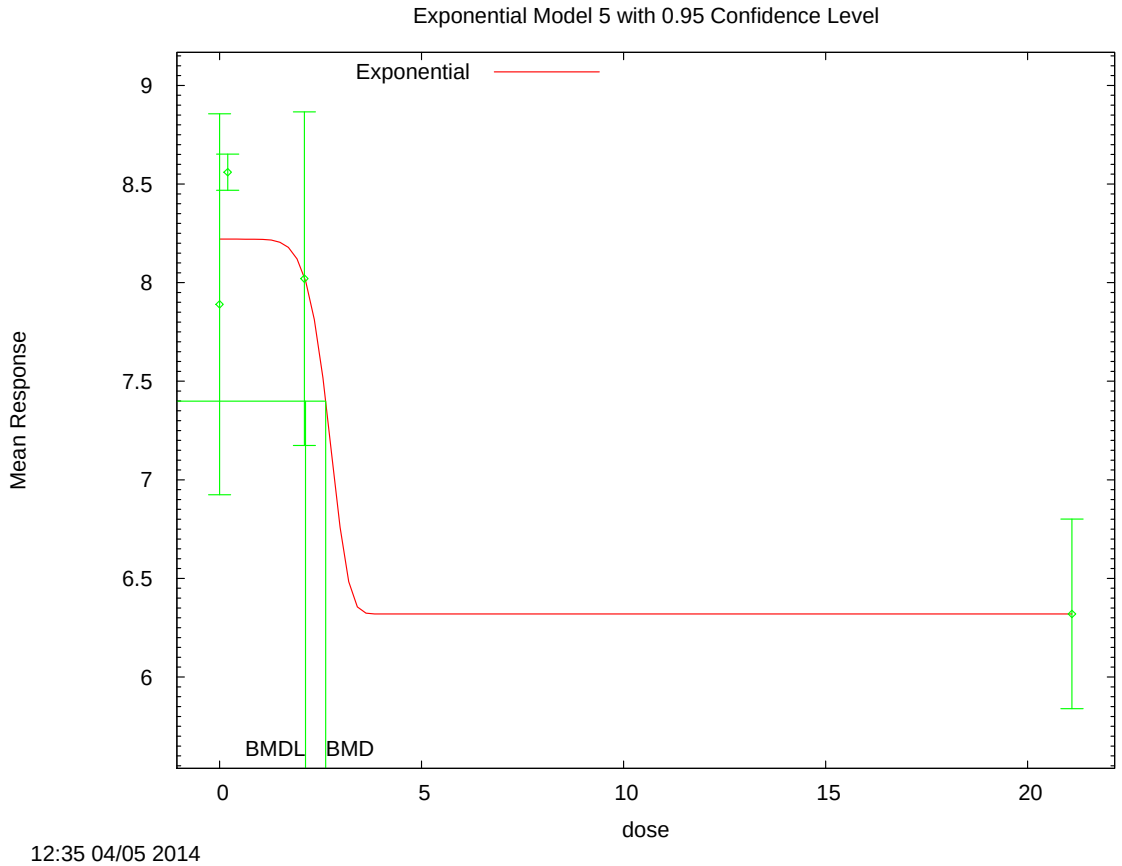
12:35 04/05 2014



12:35 04/05 2014



12:35 04/05 2014



12:35 04/05 2014

MRID 43608201 -Subchronic Neurotoxicity Female Hippocampus
CONSTANT VARIANCE - NO

```
 ======================================================================
        Exponential Model. (Version: 1.7;  Date: 12/10/2009)
        Input Data File: C:/Users/EHolman/Desktop/HED Desktop/BMDS220/Data/exp_Subchr
Neuro Female Hippocampus_Setting.(d)
        Gnuplot Plotting File:
                                                Sat Apr 05 14:25:42 2014
 ======================================================================

 BMDS Model Run
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   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   The variance is to be modeled as Var(i) = exp(lalpha + log(mean(i)) * rho)

   Total number of dose groups = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 250
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha          -6.11312          -6.11312           -6.11312          -6.11312
         rho            3.3744            3.3744             3.3744            3.3744
           a            4.5329            4.5329             7.182             7.182
           b         0.0272585         0.0272585          0.130273          0.130273
           c                --                --              0.445558
0.445558
           d                --                 1                  --                 1


                               Parameter Estimates by Model

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
```

lnalpha	-7.54006	-7.54006	-7.69685	-7.69685
rho	4.54506	4.54506	4.56301	4.56301
a	6.57182	6.57182	6.97402	6.97402
b	0.0271746	0.0271746	0.188893	0.188893
c	--	--	0.479482	0.479482
d	--	1	--	1

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	5	6.84	3.007
0.2	5	6.38	0.709
2.4	5	6.06	0.513
24.7	5	3.36	0.423

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	6.572	1.663	0.3606
	0.2	6.536	1.643	-0.2126
	2.4	6.157	1.434	-0.1511
	24.7	3.359	0.3618	0.007527
3	0	6.572	1.663	0.3606
	0.2	6.536	1.643	-0.2126
	2.4	6.157	1.434	-0.1511
	24.7	3.359	0.3618	0.007528
4	0	6.974	1.791	-0.1673
	0.2	6.839	1.713	-0.5997
	2.4	5.651	1.108	0.8256
	24.7	3.378	0.3426	-0.118
5	0	6.974	1.791	-0.1673
	0.2	6.839	1.713	-0.5997
	2.4	5.651	1.108	0.8256
	24.7	3.378	0.3426	-0.118

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC
A1	-16.91829	5	43.83658
A2	-3.914468	8	23.82894
A3	-8.844871	6	29.68974

R	-23.44838	2	50.89676
2	-11.74377	4	31.48754
3	-11.74377	4	31.48754
4	-10.76246	5	31.52491
5	-10.76246	5	31.52491

Additive constant for all log-likelihoods = -18.38. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	39.07	6	< 0.0001
Test 2	26.01	3	< 0.0001
Test 3	9.861	2	0.007224
Test 4	5.798	2	0.05508
Test 5a	5.798	2	0.05508
Test 5b	-1.901e-012	0	N/A
Test 6a	3.835	1	0.05019
Test 6b	1.963	1	0.1612
Test 7a	3.835	1	0.05019
Test 7b	1.963	1	0.1612
Test 7c	1.776e-014	0	N/A

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is less than .1. A non-homogeneous variance model appears to be appropriate.

The p-value for Test 3 is less than .1. You may want to consider a different variance model.

The p-value for Test 4 is less than .1. Model 2 may not adequately describe the data; you may want to consider another model.

The p-value for Test 5a is less than .1. Model 3 may not adequately describe the data; you may want to consider another model.

Degrees of freedom for Test 5b are less than or equal to 0.
The Chi-Square test for fit is not valid.

The p-value for Test 6a is less than .1. Model 4 may not adequately describe the data; you may want to consider another model.

The p-value for Test 6b is greater than .05. Model 4 does not seem to fit the data better than Model 2.

The p-value for Test 7a is less than .1. Model 5 may not adequately describe the data; you may want to consider another model.

The p-value for Test 7b is greater than .05. Model 5 does not seem to fit the data better than Model 3.

Degrees of freedom for Test 7c are less than or equal to 0.
The Chi-Square test for fit is not valid.

Benchmark Dose Computations:

Specified Effect = 0.100000

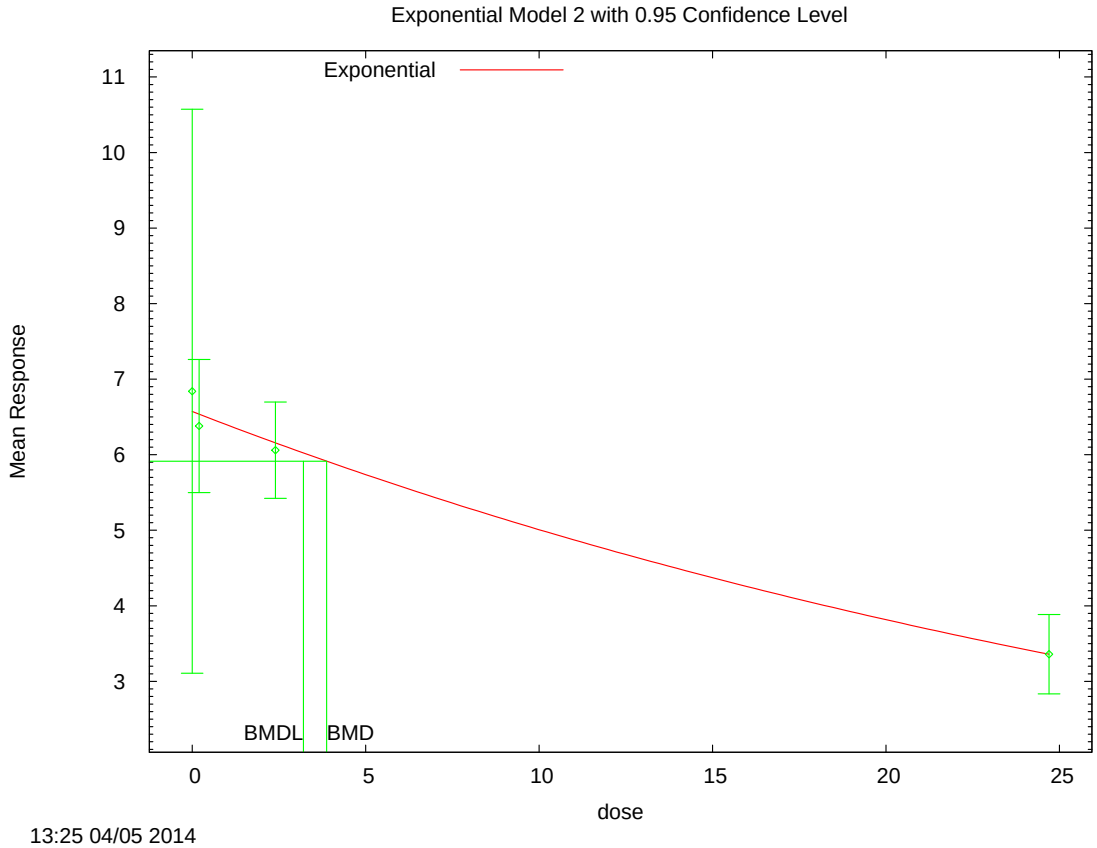
Risk Type = Relative deviation

Confidence Level = 0.950000

BMD and BMDL by Model

Model	BMD	BMDL
2	3.87717	3.20933
3	3.87717	3.20933
4	1.12941	0.577362
5	1.12941	0.577362

NO ADEQUATE FIT



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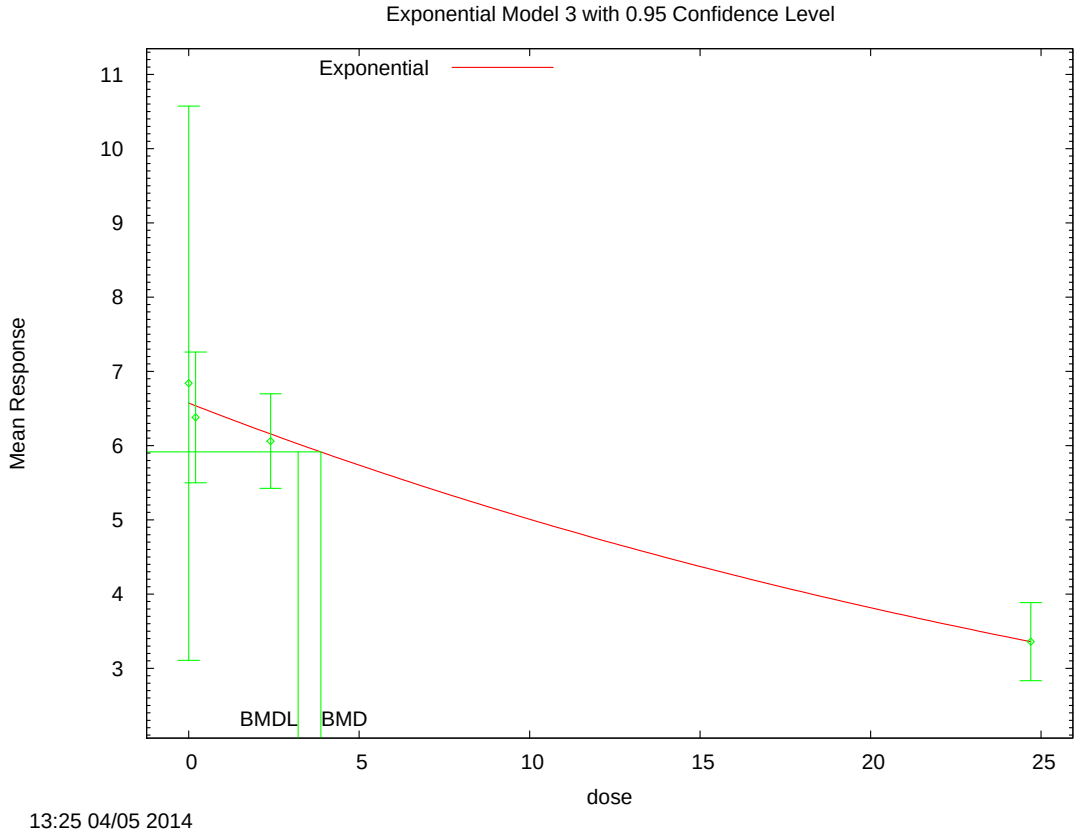

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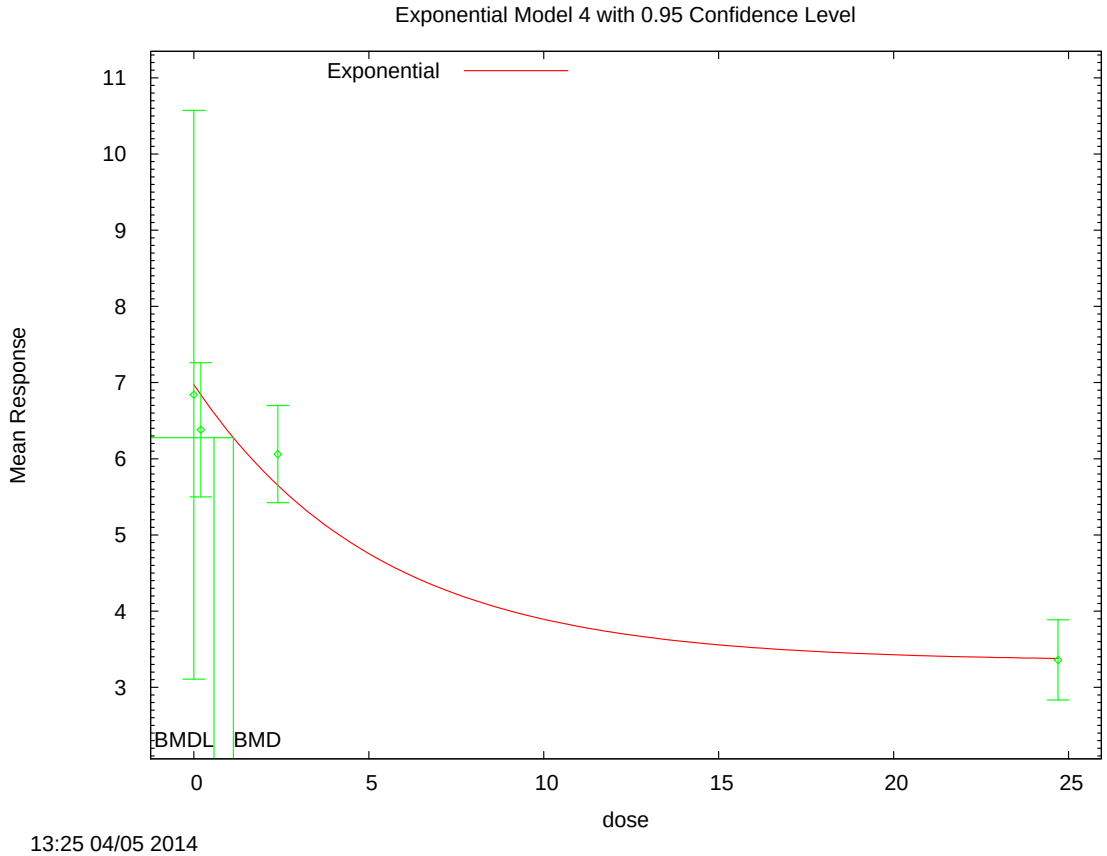

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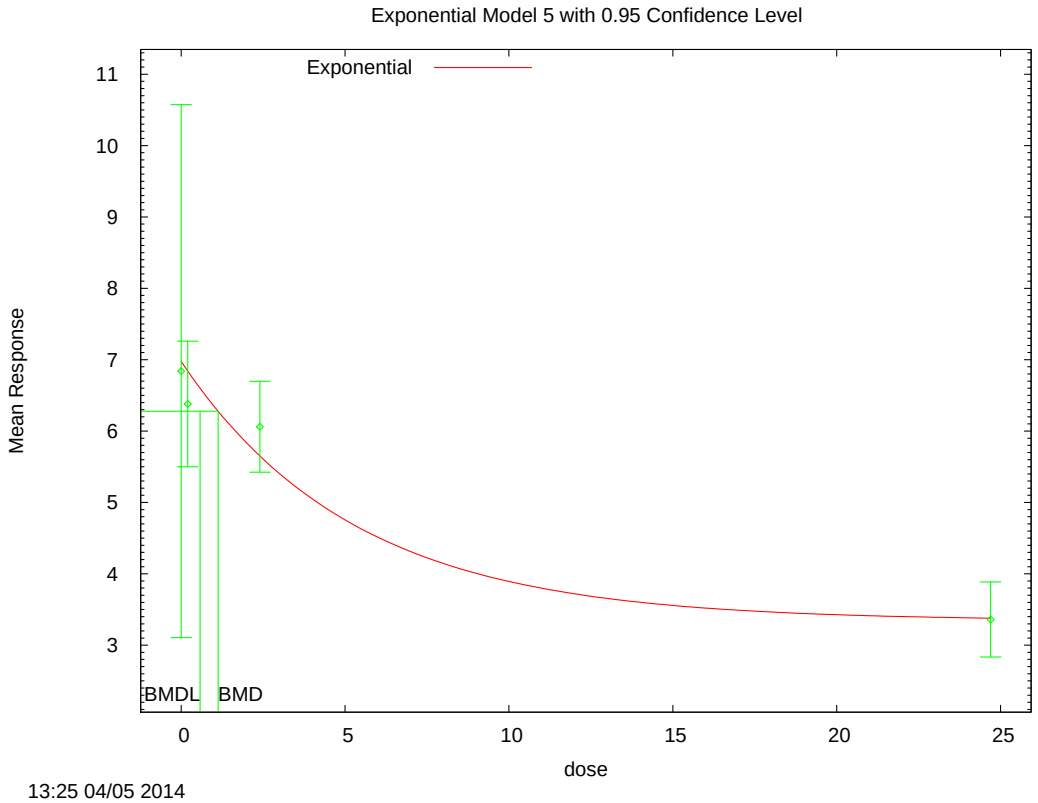

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MRID 432106301 Developmental Toxicity Study in Rabbits – Day 19

```
 ======================================================================
        Exponential Model. (Version: 1.9;  Date: 01/29/2013)
        Input Data File: F:/Pirimiphos-methyl/BMD runs/Chronic Runs/exp_Developmental
Tox Rabbit RBC Day 19_Setting.(d)
        Gnuplot Plotting File:
                                              Wed Apr 30 16:00:36 2014
 ======================================================================

 BMDS Model Run
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~

   The form of the response function by Model:
      Model 2:     Y[dose] = a * exp{sign * b * dose}
      Model 3:     Y[dose] = a * exp{sign * (b * dose)^d}
      Model 4:     Y[dose] = a * [c-(c-1) * exp{-b * dose}]
      Model 5:     Y[dose] = a * [c-(c-1) * exp{-(b * dose)^d}]

    Note: Y[dose] is the median response for exposure = dose;
          sign = +1 for increasing trend in data;
          sign = -1 for decreasing trend.

      Model 2 is nested within Models 3 and 4.
      Model 3 is nested within Model 5.
      Model 4 is nested within Model 5.


   Dependent variable = Mean
   Independent variable = Dose
   Data are assumed to be distributed: normally
   Variance Model: exp(lnalpha +rho *ln(Y[dose]))
   rho is set to 0.
   A constant variance model is fit.

   Total number of dose groups = 4
   Total number of records with missing values = 0
   Maximum number of iterations = 500
   Relative Function Convergence has been set to: 1e-008
   Parameter Convergence has been set to: 1e-008

   MLE solution provided: Exact


                                Initial Parameter Values

     Variable          Model 2           Model 3           Model 4           Model 5
     --------          -------           -------           -------           -------
     lnalpha           11.2542           11.2542             11.2542           11.2542
         rho(S)              0                 0                   0                 0
           a           680.475           680.475            1709.4            1709.4
           b         0.0203558         0.0203558           0.0320312         0.0320312
           c                --                --              0.181643
0.181643
           d                --                 1                  --                 1

     (S) = Specified
```

Parameter Estimates by Model

Variable	Model 2	Model 3	Model 4	Model 5
lnalpha	11.2741	11.2741	11.2686	11.2542
rho	0	0	0	0
a	1625.68	1625.68	1641.74	1628
b	0.0213387	0.0213387	0.0285921	0.0460467
c	--	--	0.157929	0.360907
d	--	1	--	1.55687

Table of Stats From Input Data

Dose	N	Obs Mean	Obs Std Dev
0	6	1628	352
12	6	1287	332
24	6	911	331
48	6	621	164

Estimated Values of Interest

Model	Dose	Est Mean	Est Std	Scaled Residual
2	0	1626	280.6	0.02029
	12	1258	280.6	0.2494
	24	974.1	280.6	-0.5511
	48	583.7	280.6	0.3254
3	0	1626	280.6	0.02029
	12	1258	280.6	0.2494
	24	974.1	280.6	-0.5511
	48	583.7	280.6	0.3254
4	0	1642	279.9	-0.1202
	12	1240	279.9	0.4094
	24	955.3	279.9	-0.3879
	48	609.7	279.9	0.09871
5	0	1628	277.9	1.764e-007
	12	1287	277.9	-5.261e-007
	24	911	277.9	6.058e-007
	48	621	277.9	3.277e-007

Other models for which likelihoods are calculated:

Model A1: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma^2

Model A2: Yij = Mu(i) + e(ij)
Var{e(ij)} = Sigma(i)^2

Model A3: Yij = Mu(i) + e(ij)
Var{e(ij)} = exp(lalpha + log(mean(i)) * rho)

Model R: Yij = Mu + e(i)
Var{e(ij)} = Sigma^2

Likelihoods of Interest

Model	Log(likelihood)	DF	AIC

A1	-147.0507	5	304.1013
A2	-145.2366	8	306.4733
A3	-147.0507	5	304.1013
R	-159.7142	2	323.4283
2	-147.2891	3	300.5782
3	-147.2891	3	300.5782
4	-147.2231	4	302.4461
5	-147.0507	5	304.1013

Additive constant for all log-likelihoods = -22.05. This constant added to the above values gives the log-likelihood including the term that does not depend on the model parameters.

Explanation of Tests

Test 1: Does response and/or variances differ among Dose levels? (A2 vs. R)
Test 2: Are Variances Homogeneous? (A2 vs. A1)
Test 3: Are variances adequately modeled? (A2 vs. A3)
Test 4: Does Model 2 fit the data? (A3 vs. 2)

Test 5a: Does Model 3 fit the data? (A3 vs 3)
Test 5b: Is Model 3 better than Model 2? (3 vs. 2)

Test 6a: Does Model 4 fit the data? (A3 vs 4)
Test 6b: Is Model 4 better than Model 2? (4 vs. 2)

Test 7a: Does Model 5 fit the data? (A3 vs 5)
Test 7b: Is Model 5 better than Model 3? (5 vs. 3)
Test 7c: Is Model 5 better than Model 4? (5 vs. 4)

Tests of Interest

Test	-2*log(Likelihood Ratio)	D. F.	p-value
Test 1	28.96	6	< 0.0001
Test 2	3.628	3	0.3045
Test 3	3.628	3	0.3045
Test 4	0.4769	2	0.7878
Test 5a	0.4769	2	0.7878
Test 5b	5.684e-014	0	N/A
Test 6a	0.3448	1	0.5571
Test 6b	0.1321	1	0.7162
Test 7a	9.663e-013	0	N/A
Test 7b	0.4769	2	0.7878
Test 7c	0.3448	1	0.5571

The p-value for Test 1 is less than .05. There appears to be a difference between response and/or variances among the dose levels, it seems appropriate to model the data.

The p-value for Test 2 is greater than .1. A homogeneous variance model appears to be appropriate here.

The p-value for Test 3 is greater than .1. The modeled variance appears to be appropriate here.

The p-value for Test 4 is greater than .1. Model 2 seems to adequately describe the data.

The p-value for Test 5a is greater than .1. Model 3 seems to adequately describe the data.

Degrees of freedom for Test 5b are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 6a is greater than .1. Model 4 seems to adequately describe the data.

The p-value for Test 6b is greater than .05. Model 4 does not seem to fit the data better than Model 2.

Degrees of freedom for Test 7a are less than or equal to 0. The Chi-Square test for fit is not valid.

The p-value for Test 7b is greater than .05. Model 5 does not seem to fit the data better than Model 3.

The p-value for Test 7c is greater than .05. Model 5 does not seem to fit the data better than Model 4.

Benchmark Dose Computations:

Specified Effect = 0.100000

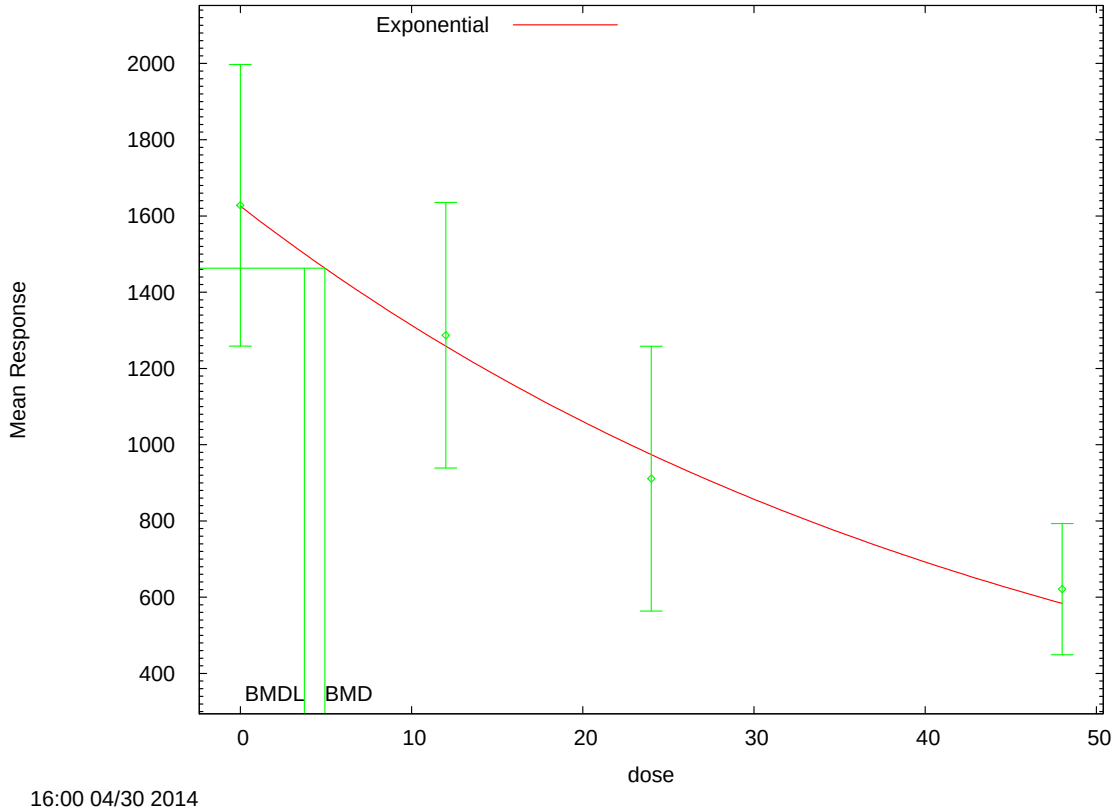
Risk Type = Relative deviation

Confidence Level = 0.950000

BMD and BMDL by Model

Model	BMD	BMDL
2	4.93754	3.74662
3	4.93754	3.74662
4	4.42149	2.58979
5	6.96263	2.68443

Exponential Model 2, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



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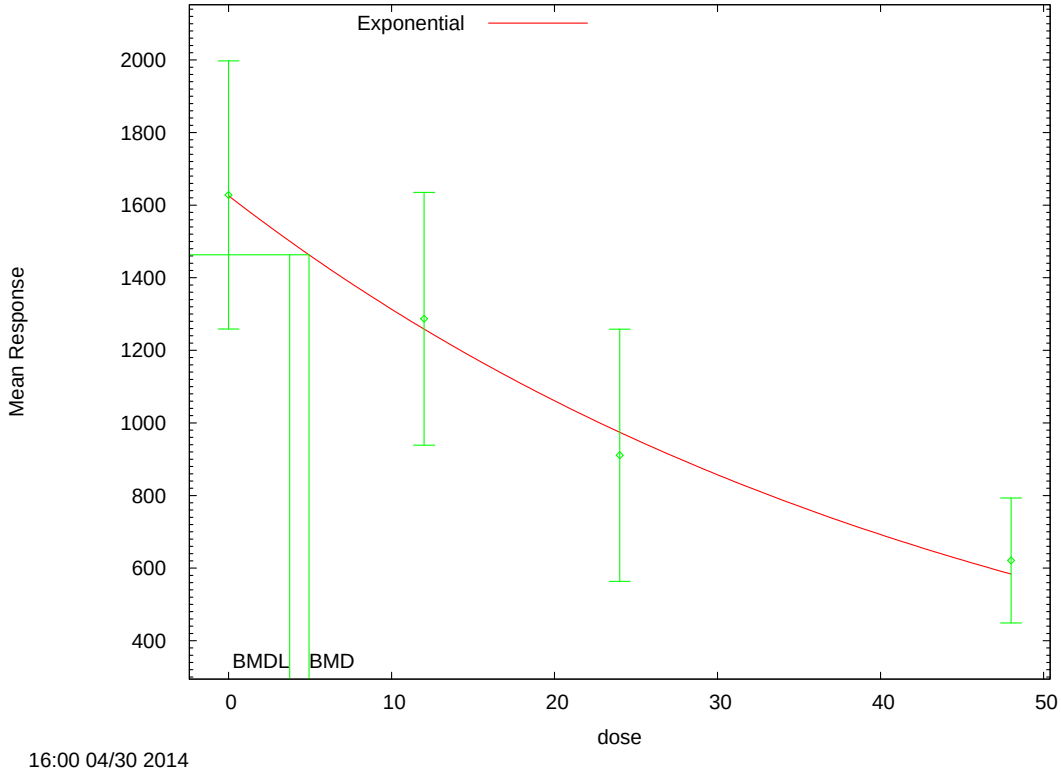
Exponential Model 3, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



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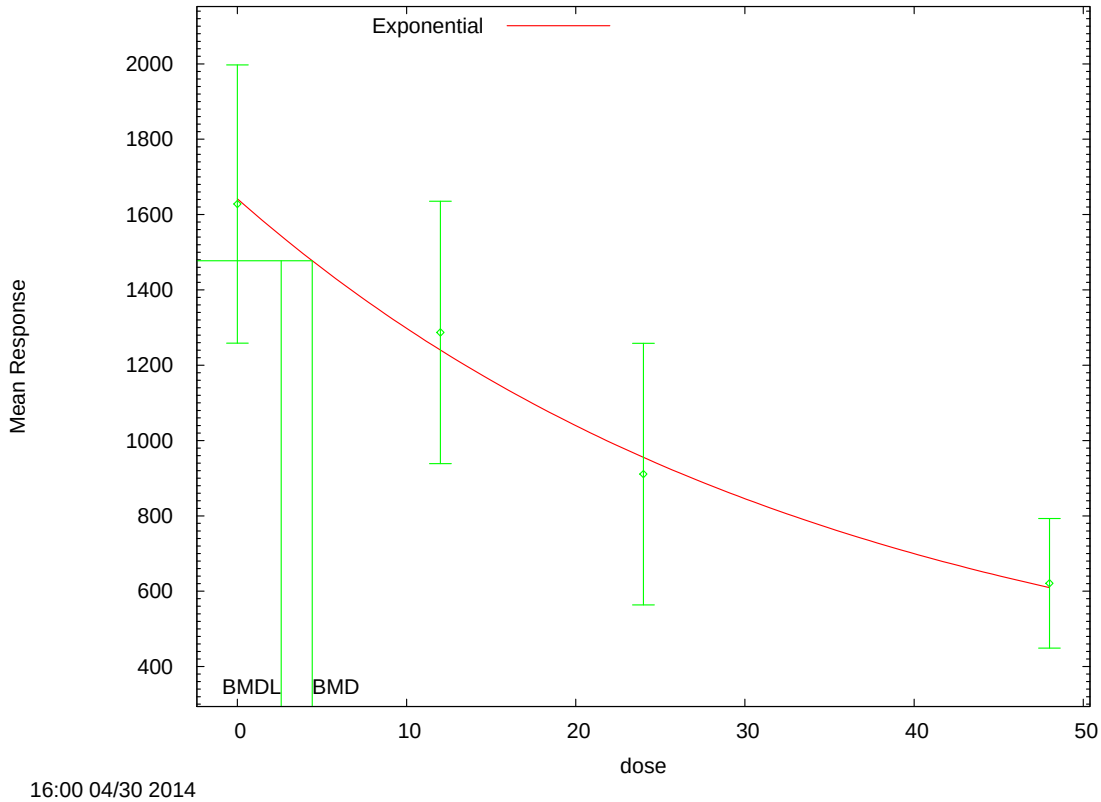
Exponential Model 4, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



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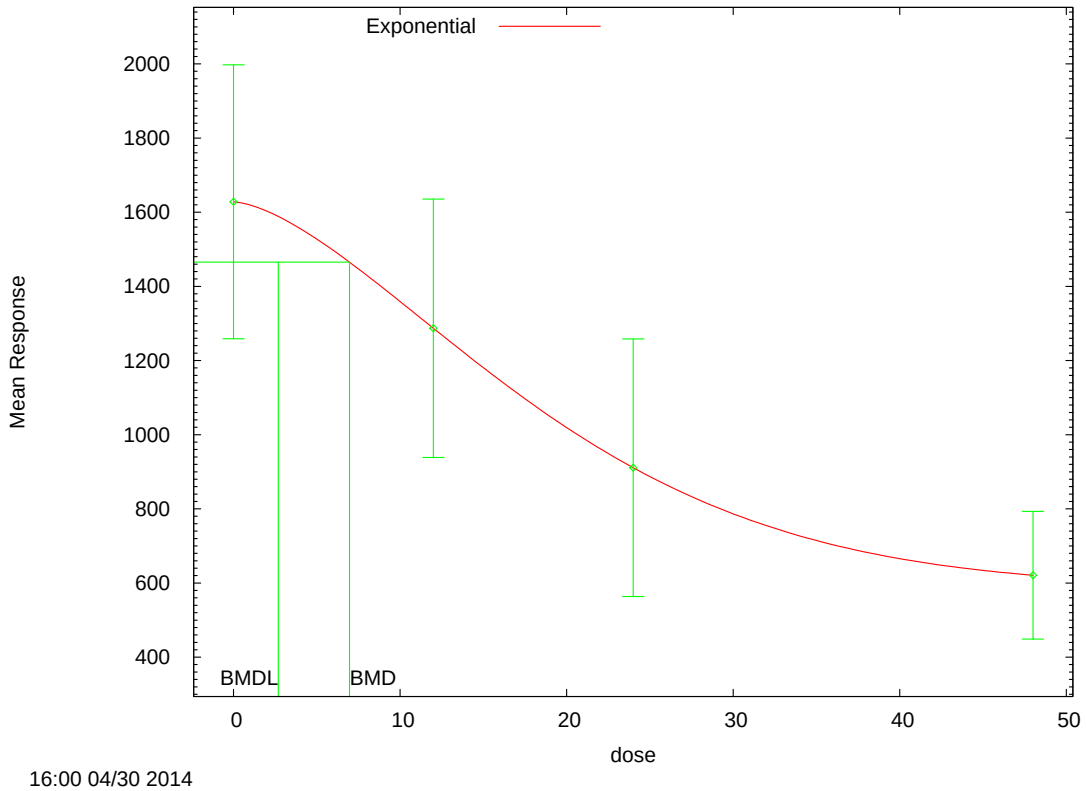
Exponential Model 5, with BMR of 0.1 Rel. Dev. for the BMD and 0.95 Lower Confidence Level for BMDL



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